MAXIMUM DOSAGE POLICY

Policy Number: PHARMACY 259.11 T1 **Effective Date**: April 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.

BENEFIT CONSIDERATIONS

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

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 plan 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 when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to: Acquired Rare Disease Drug Therapy Exception Process.

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

This policy provides information about the maximum dosage per administration for certain medications administered by a medical professional.

Drug Products:

- bevacizumab (Avastin®)
- eculizumab (Soliris®)
- infliximab (Remicade®)
- infliximab-dyyb (Inflectra™)
- infliximab-abda (Renflexis™)
- omalizumab (Xolair®)
- pegfilgrastim (Neulasta®)
- rituximab (Rituxan®)
- trastuzumab (Herceptin®)
- ustekinumab (Stelara®)
- vedolizumab (Entyvio®)
- zoledronic acid (zoledronic acid, Reclast® and Zometa®)

Most medications have a maximum dosage based upon body surface area or patient weight or a set maximal dosage independent of patient body size, and are proven when used according to labeled indications or when otherwise supported by published clinical evidence. The medications included in this policy when given beyond maximum dosages based upon body surface area or patient weight or a set maximal dosage independent of patient body size are not supported by package labeling or published clinical evidence and are not medically necessary.

This policy creates an upper dose limit based on the clinical evidence and the 95th percentile for adult body weight (119 kg) and body surface area (2.45 meters^2) in the U.S. (Fryar, 2012). In some cases, the maximum allowed units and/or vials may exceed the upper level limit as defined within this policy due to an individual patient body weight > 119 kg or body surface area > 2.45 meters^2.

HCPCS Code Based Maximum Dosage Information

Medication Name		Diagnosis	Maximum Dosage Per Administration	HCPCS Code	Maximum Allowed
Brand	Generic				
Avastin	bevacizumab		15 mg/kg	J9035	179 HCPCS units (10 mg per unit)
Entyvio	vedolizumab		300 mg	J3380	300 HCPCS units (1 mg per unit)
Herceptin	trastuzumab		8 mg/kg	J9355	95 HCPCS units (10 mg per unit)
Neulasta	pegfilgrastim		6 mg total dose	J2505	1 HCPCS unit (6 mg per unit)
Reclast	zoledronic acid		5 mg total dose	J3489	5 HCPCS units (1 mg per unit)
Zoledronic Acid	zoledronic acid		5 mg total dose		
			4 mg total dose		
Zometa	zoledronic acid		4 mg total dose		
Remicade	infliximab		10 mg/kg	J1745	119 HCPCS units (10 mg per unit)
Inflectra	infliximab-dyyb		10 mg/kg	Q5103	119 HCPCS units (10 mg per unit)

Medication Name		Diagnosis	Maximum Dosage Per Administration	HCPCS Code	Maximum Allowed
Brand	Generic				
Renflexis	infliximab-abda		10 mg/kg	Q5104	119 HCPCS units (10 mg per unit)
Rituxan	rituximab		1,225 mg total dose	J9310	13 HCPCS units (100 mg per unit)
Soliris	eculizumab	PNH	900 mg	J1300	90 HCPCS units (10 mg per unit)
		aHUS, MG	1200 mg	J1300	120 HCPCS units (10 mg per unit)
Stelara	ustekinumab		90 mg	J3357	90 HCPCS units (1 mg per unit)
		Crohn's Disease	520 mg	J3358	520 HCPCS units (1 mg per unit)
Xolair	omalizumab	Asthma	375 mg	J2357	90 HCPCS units (5 mg per unit)
		Chronic Urticaria	300 mg	J2357	60 HCPCS units (5 mg per unit)

Maximum Allowed Quantities for National Drug Code (NDC) Billing

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDC's for each drug product and is subject to change.

Medication Name		Diagnosis	How Supplied	National Drug Code	Maximum Allowed
Brand	Generic				
Avastin	Bevacizumab		100 mg/4mL solution in vials	50242-0060-01	72 mL
			400 mg/16 mL solution in vials	50242-0061-01	72 mL
Entyvio	Vedolizumab		300 mg powder for reconstitution	64764-0300-20	1 vial
Herceptin	trastuzumab		440 mg powder for reconstitution	50242-0056-56	3 vials
				50242-0134-68	3 vials
Inflectra	infliximab-dyyb		100 mg powder for reconstitution	32228-0001-01	12 vials
Neulasta	pegfilgrastim		6 mg/0.6 mL prefilled syringe	54868-5229-00	0.6 mL
				55513-0190-01	0.6 mL
			6 mg/0.6 mL prefilled syringe with on-body Injector	55513-0190-01	0.6 mL
Reclast	zoledronic acid		5 mg/100 mL solution in vials	00078-0435-61	100 mL
				35356-0351-01	100 mL
Remicade	infliximab		100 mg powder for reconstitution	57894-0030-01	12 vials
Renflexis	infliximab-abda		100 mg powder for reconstitution	00006-4305-02	12 vials
Rituxan	rituximab		100 mg/10 mL solution in vials	50242-0051-21	130 mL
			500 mg/50 mL solution in vials	50242-0053-06	130 mL
Soliris	eculizumab	PNH	300 mg/30 mL solution in vials	25682-0001-01	3 vials
		aHUS, MG	300 mg/30 mL solution in vials	25682-0001-01	4 vials
Stelara	ustekinumab		45 mg/0.5 mL prefilled syringe	57894-0060-03	0.5 mL
			45 mg/0.5 mL solution in vials	57894-0060-02	0.5 mL
			90 mg/1 mL prefilled syringe	57894-0061-03	1 mL
		Crohn's Disease	130 mg/26 mL solution in vials	57894-0054-27	104 mL

Medication Name		Diagnosis	How Supplied	National Drug Code	Maximum Allowed
Brand	Generic				
Xolair	omalizumab	Asthma	150 mg powder for reconstitution	50242-0040-62	3 vials
		Chronic Urticaria	150 mg powder for reconstitution	50242-0040-62	2 vials
Zoledronic Acid	zoledronic acid		5 mg/100 mL solution in vials	25021-0830-82 42023-0163-01 43598-0331-11 23155-0186-31 55111-0688-52	100 mL
			4 mg/5 mL solution in vials	00143-9642-01 47335-0035-40 25021-0801-66 42023-0151-01 43598-0330-11 53150-0871-01 23155-0170-31 55111-0685-07 60505-6110-00 45963-0440-55	5 mL
			4 mg/5 ml lyophilisate for solution for injection in vials	47335-0962-41	5 mL
			4 mg/100 mL solution in vials	25021-0826-82	100 mL
Zometa	zoledronic acid		4 mg/5 mL solution in vials	00078-0387-25	5 mL
			4 mg/100 mL solution in vials	00078-0590-61	100 mL

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.

HCPCS Code	Description
J1300	Injection, eculizumab, 10 mg
J1745	Injection, infliximab, excludes biosimilar, 10 mg
J2357	Injection, omalizumab, 5 mg
J2505	Injection, pegfilgrastim, 6 mg
J3357	Ustekinumab, for subcutaneous injection, 1mg
J3358	Ustekinumab, for intravenous injection, 1 mg
J3380	Injection, vedolizumab, 1 mg
J3489	Injection, zoledronic acid, 1 mg
J9035	Injection, bevacizumab, 10 mg
J9310	Injection, rituximab, 100 mg
J9355	Injection, trastuzumab, 10 mg
Q5103	Injection, Infliximab-dyyb, biosimilar, (Inflectra), 10 mg
Q5104	Injection, Infliximab-abda, biosimilar, (Renflexis), 10 mg

National Drug Code	Description
50242-0060-01	Avastin 100 mg/4 mL solution in vials
50242-0061-01	Avastin 400 mg/16 mL solution in vials
64764-0300-20	Entyvio 300 mg powder for reconstitution
50242-0056-56	Herceptin 440 mg powder for reconstitution

National Drug Code	Description
50242-0134-68	Herceptin 440 mg powder for reconstitution
32228-0001-01	Inflectra 100 mg powder for reconstitution
55513-0190-01	Neulasta 6 mg/0.6 mL prefilled syringe
54868-5229-00	Neulasta 6 mg/0.6 mL prefilled syringe
00078-0435-61	Reclast 5 mg/100 mL solution in vials
35356-0351-01	Reclast 5 mg/100 mL solution in vials
57894-0030-01	Remicade 100 mg powder for reconstitution
00006-4305-02	Renflexis 100 mg powder for reconstitution
50242-0051-21	Rituxan 100 mg/10 mL solution in vials
50242-0053-06	Rituxan 500 mg/50 mL solution in vials
25682-0001-01	Soliris 300 mg/30 mL solution in vials
57894-0054-27	Stelara 130 mg/26 mL solution in vials
57894-0060-03	Stelara 45 mg/0.5 mL prefilled syringe
57894-0060-02	Stelara 45 mg/0.5 mL solution in vials
57894-0061-03	Stelara 90 mg/1 mL prefilled syringe
50242-0040-62	Xolair 150 mg powder for reconstitution
25021-0826-82	Zoledronic Acid 4 mg/100 mL solution in vials
47335-0962-41	Zoledronic Acid 4 mg/5 ml lyophilisate for solution for injection in vials
00143-9642-01	Zoledronic Acid 4 mg/5 mL solution in vials
47335-0035-40	Zoledronic Acid 4 mg/5 mL solution in vials
25021-0801-66	Zoledronic Acid 4 mg/5 mL solution in vials
42023-0151-01	Zoledronic Acid 4 mg/5 mL solution in vials
43598-0330-11	Zoledronic Acid 4 mg/5 mL solution in vials
53150-0871-01	Zoledronic Acid 4 mg/5 mL solution in vials
23155-0170-31	Zoledronic Acid 4 mg/5 mL solution in vials
55111-0685-07	Zoledronic Acid 4 mg/5 mL solution in vials
60505-6110-00	Zoledronic Acid 4 mg/5 mL solution in vials
45963-0440-55	Zoledronic Acid 4 mg/5 mL solution in vials
25021-0830-82	Zoledronic Acid 5 mg/100 mL solution in vials
42023-0163-01	Zoledronic Acid 5 mg/100 mL solution in vials
43598-0331-11	Zoledronic Acid 5 mg/100 mL solution in vials
23155-0186-31	Zoledronic Acid 5 mg/100 mL solution in vials
55111-0688-52	Zoledronic Acid 5 mg/100 mL solution in vials
00078-0590-61	Zometa 4 mg/100 mL solution in vials
00078-0387-25	Zometa 4 mg/5 mL solution in vials

CLINICAL EVIDENCE

The aforementioned pharmaceuticals all have dosing parameters that support a maximum dosage per body weight or body surface area or a set maximal dosage independent of patient body size. These maximum doses are product-specific, and in some cases, disease state-specific and are defined in the U.S. Food and Drug Administration (FDA) approved product prescribing information and/or in national compendia and other peer reviewed resources. This policy creates an upper dose limit based on the clinical evidence and the 95th percentile for adult body weight (119 kg) and body surface area (2.45 meters^2) in the U.S. (Fryar, 2012)

Clinical evidence supports the use of the medications listed in this policy up to maximum dosages based upon body surface area or patient weight, when used according to labeled indications or when otherwise supported by published clinical evidence.

Clinical evidence does not support the use of the medications listed in this policy beyond maximum dosages based upon body surface area or patient weight. Use of these agents beyond such established maximum dosages adds significantly to risk of adverse events without conferring additional clinical benefit.

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy, Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee. [*2017D0034N*]

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15. Soliris [prescribing information]. New Haven, CT: Alexion Pharmaceuticals, Inc.; January 2017.
16. Renflexis [prescribing information]. Kenilworth, NJ: Merck Sharp & Dohme Corp; April 2017.
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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
04/01/2018	• Updated coverage rationale; modified HCPCS code based maximum dosage information to reflect quarterly code edits for: **Inflectra (infliximab-dyyb)** ○ Added Q5013 ○ Removed Q5102 **Renflexis (infliximab-abda)** ○ Added Q5104 ○ Removed Q5102 • Updated list of applicable HCPCS codes to reflect quarterly code edits: ○ Added Q5103 and Q5104 ○ Removed Q5102 • Archived previous policy version PHARMACY 259.10 T1