



Topical Estrogen Quantity Limit Program Summary

Quantity limits apply to Medicaid.

POLICY REVIEW CYCLE

Effective Date
2/1/2024

Date of Origin
5/1/2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
ALORA® (estradiol) Transdermal system*	<p>Treatment of moderate to severe vasomotor symptoms associated with the menopause</p> <p>Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause</p> <ul style="list-style-type: none"> Limitation of use: When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, first consider the use of topical vaginal products. <p>Treatment of hypoestrogenism due to hypogonadism, castration or primary ovarian failure</p> <p>Prevention of postmenopausal osteoporosis</p> <ul style="list-style-type: none"> Limitation of use: When prescribing solely for the prevention of postmenopausal osteoporosis, only consider therapy for women at significant risk of osteoporosis. First consider the use of non-estrogen medications. 	*generic available	3
Climara® (estradiol) Transdermal system*	<p>Treatment of moderate to severe vasomotor symptoms due to menopause</p> <p>Treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause</p> <ul style="list-style-type: none"> Limitation of use: When prescribing solely for the treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause, first consider the use of topical vaginal products. <p>Treatment of hypoestrogenism due to hypogonadism, castration, or primary ovarian failure</p> <p>Prevention of postmenopausal osteoporosis</p> <ul style="list-style-type: none"> Limitation of use: When prescribing solely for the prevention of postmenopausal osteoporosis, first consider the use of non-estrogen medications. Consider estrogen therapy only for women at significant risk of osteoporosis. 	*generic available	4
Climara Pro®	Treatment of moderate to severe vasomotor symptoms due to menopause in women with a uterus		5

Agent(s)	FDA Indication(s)	Notes	Ref#
(estradiol/levonorgestrel) Transdermal System	Prevention of postmenopausal osteoporosis in women with a uterus <ul style="list-style-type: none"> Limitation of use: When prescribing solely for the prevention of postmenopausal osteoporosis, first consider the use of non-estrogen medications. Consider estrogen therapy only for women at significant risk of osteoporosis. 		
CombiPatch® (estradiol/norethindrone) Transdermal System	Treatment in women with a uterus for: <ul style="list-style-type: none"> Moderate to severe vasomotor symptoms due to menopause Moderate to severe symptoms of vulvar and vaginal atrophy due to menopause Hypoenestrogenism due to hypogonadism, castration, or primary ovarian failure 		6
Divigel® (estradiol) Gel*	Treatment of moderate to severe vasomotor symptoms due to menopause	*generic available	7
Elestrin® (estradiol) Topical Gel	Treatment of moderate to severe vasomotor symptoms due to menopause		8
ESTRACE® (estradiol) Vaginal Cream*	Treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause	*generic available	17
Estring® (estradiol) Vaginal Ring	Treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause		9
EstroGel® (estradiol) Topical Gel	Treatment of moderate to severe vasomotor symptoms due to menopause Treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause <ul style="list-style-type: none"> Limitation of Use: When prescribing solely for the treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause, first consider the use of topical vaginal products. 		10
Evamist® (estradiol) Transdermal Spray	Treatment of moderate to severe vasomotor symptoms due to menopause		11

Agent(s)	FDA Indication(s)	Notes	Ref#
Femring® (estradiol) Vaginal Ring	Treatment of moderate to severe vasomotor symptoms due to menopause Treatment of moderate to severe vulvar and vaginal atrophy due to menopause		12
Imvexxy® (estradiol) Vaginal Insert	Treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause		13
MENOSTAR® (estradiol) Transdermal System	Prevention of postmenopausal osteoporosis Limitation of use: When prescribing solely for the prevention of postmenopausal osteoporosis, first consider the use of non-estrogen medication. Consider estrogen therapy only for women at significant risk of osteoporosis.		14
Minivelle® (estradiol) Transdermal System*	Treatment of moderate to severe vasomotor symptoms due to menopause Prevention of postmenopausal osteoporosis <ul style="list-style-type: none"> Limitation of Use: When prescribing solely for the prevention of postmenopausal osteoporosis, first consider the use of non-estrogen medications. Consider estrogen therapy only for women at significant risk of osteoporosis. 	*generic available	15
Vivelle-Dot® (estradiol) Transdermal System*	Treatment of moderate to severe vasomotor symptoms due to menopause Treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause <ul style="list-style-type: none"> Limitation of Use: When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered. Treatment of hypoestrogenism due to hypogonadism, castration, or primary ovarian failure Prevention of postmenopausal osteoporosis <ul style="list-style-type: none"> Limitation of Use: When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and non-estrogen medications should be carefully considered. 	*generic available	16

See package insert for FDA prescribing information: <https://dailymed.nlm.nih.gov/dailymed/index.cfm>

CLINICAL RATIONALE

Overview	Menopause, defined as one year without menses, typically occurs around the age of 50 in most women and is due to the ovary's loss of estrogen production. Estrogen deficiency can often be asymptomatic, but can be associated with vasomotor symptoms (e.g., hot flashes, sweating, insomnia, vaginal dryness). Estrogen therapy, with or without progestin, is considered the most effective therapy for menopausal
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	<p>vasomotor symptoms. The American Association of Clinical Endocrinologists (AACE) recommend transdermal estrogen therapy to avoid the risk of first-pass effect and potentially reduce the risk of thromboembolic events. Transvaginal estrogen may be considered to provide topical effects with less systemic absorption. AACE also recommend that hormone therapy (HT) should be used at the lowest dose possible, the dose should be decreased as the patient ages, and should be used for the shortest duration necessary to control menopausal symptoms.(1)</p> <p>Estrogens are also recommended as adjunct therapy to treat gender dysphoric/gender incongruence. The Endocrine Society recommends the use of oral, transdermal, and injectable estrogen. Transdermal estrogen should be used at doses between 0.025-0.2 mg/day.(2)</p>
Safety	<p>Topical estradiol has a boxed warning due to endometrial cancer, cardiovascular disorders, probable dementia, and breast cancer. See full prescribing information for complete boxed warning.(3-17)</p> <p>Estrogen-Alone Therapy</p> <ul style="list-style-type: none"> • There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens • Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia • The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) • The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age or older <p>Estrogen Plus Progestin Therapy</p> <ul style="list-style-type: none"> • Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia • The WHI estrogen plus progestin substudy reported increased risks of stroke, DVT, pulmonary embolism (PE), and myocardial infarction (MI) • The WHI estrogen plus progestin substudy reported increased risks of invasive breast cancer • The WHIMS estrogen plus progestin ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older <p>EvaMist also has a boxed warning due to unintentional secondary exposure.(11)</p> <ul style="list-style-type: none"> • Breast budding, breast masses, and gynecomastia have been reported in children following unintentional secondary exposure to Evamist <p>Topical estradiol is contraindicated in patients with:(3-17)</p> <ul style="list-style-type: none"> • Undiagnosed abnormal genital bleeding • Breast cancer or history of breast cancer • Estrogen-dependent neoplasia • Active DVT, PE, or a history of these conditions • Active arterial thromboembolic disease (e.g., stroke and MI) or a history of these conditions • Known anaphylactic reaction, angioedema, or hypersensitivity to the inactive or active ingredients in the product • Hepatic impairment or disease • Protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders

Combipatch, Estrace, Estring, EvaMist, and Femring are also contraindication in patients with known or suspected pregnancy.(6,9,11,12,17)

REFERENCES

Number	Reference
1	Rhoda H. Cobin and Neil F. Goodman (2017) American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on Menopause–2017 Update. Endocrine Practice: July 2017, Vol. 23, No. 7, pp. 869-881.
2	Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017;102:3869–3903.
3	Alora prescribing information. Allergan USA, Inc. March 2020.
4	Climara prescribing information. Bayer HealthCare Pharmaceuticals, Inc. September 2021.
5	Climara Pro prescribing information. Bayer HealthCare Pharmaceuticals, Inc. November 2021.
6	CombiPatch prescribing information. Noven Pharmaceuticals, Inc. December 2021.
7	Divigel prescribing information. Vertical Pharmaceuticals, Inc. April 2022.
8	Elestrin prescribing information. MEDA Pharmaceuticals. October 2020.
9	Estring prescribing information. Pharmacia & Upjohn Company, LLC. December 2021.
10	Estrogel prescribing information. Ascend Pharmaceuticals, LLC. December 2021.
11	EvaMist prescribing information. Padagis US, LLC. August 2021.
12	Femring prescribing information. Millicent Pharma Limited. August 2018.
13	Imvexxy prescribing information. Therapeutics MD, Inc. November 2021.
14	Menostar prescribing information. Bayer HealthCare Pharmaceuticals, Inc. September 2021.
15	Minivelle prescribing information. Noven Pharmaceuticals, Inc. October 2021.
16	Vivelle Dot prescribing information. Novartis Pharmaceuticals Corporation. October 2021.
17	Estrace Cream prescribing information. Allergan USA, Inc. December 2022.

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.025 MG/24HR	0.025 MG/24HR	8	Patches	28	DAYS			
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.05 MG/24HR	0.05 MG/24HR	8	Patches	28	DAYS			
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.075 MG/24HR	0.075 MG/24HR	8	Patches	28	DAYS			
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.1 MG/24HR	0.1 MG/24HR	8	Patches	28	DAYS			
Climara	Estradiol TD Patch Weekly 0.025 MG/24HR	0.025 MG/24HR	4	Patches	28	DAYS			
Climara	Estradiol TD Patch Weekly 0.0375	37.5 MCG/24HR	4	Patches	28	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
	MG/24HR (37.5 MCG/24HR)								
Climara	Estradiol TD Patch Weekly 0.05 MG/24HR	0.05 MG/24HR	4	Patches	28	DAYS			
Climara	Estradiol TD Patch Weekly 0.06 MG/24HR	0.06 MG/24HR	4	Patches	28	DAYS			
Climara	Estradiol TD Patch Weekly 0.075 MG/24HR	0.075 MG/24HR	4	Patches	28	DAYS			
Climara	Estradiol TD Patch Weekly 0.1 MG/24HR	0.1 MG/24HR	4	Patches	28	DAYS			
Climara pro	Estradiol-Levonorgestrel TD Patch Weekly 0.045-0.015 MG/DAY	0.045-0.015 MG/DAY	4	Patches	28	DAYS			
Combipatch	Estradiol-Norethindrone Ace TD PTTW 0.05-0.14 MG/DAY	0.05-0.14 MG/DAY	8	Patches	28	DAYS			
Combipatch	Estradiol-Norethindrone Ace TD PTTW 0.05-0.25 MG/DAY	0.05-0.25 MG/DAY	8	Patches	28	DAYS			
Divigel	Estradiol TD Gel 0.25 MG/0.25GM (0.1%)	0.25 MG/0.25 GM	30	Packets	30	DAYS			
Divigel	Estradiol TD Gel 0.5 MG/0.5GM (0.1%)	0.5 MG/0.5 GM	30	Packets	30	DAYS			
Divigel	Estradiol TD Gel 0.75 MG/0.75GM (0.1%)	0.75 MG/0.75 GM	30	Packets	30	DAYS			
Divigel	Estradiol TD Gel 1 MG/GM (0.1%)	1 MG/GM	30	Packets	30	DAYS			
Divigel	Estradiol TD Gel 1.25 MG/1.25GM (0.1%)	1.25 MG/1.25 GM	30	Packets	30	DAYS			
Dotti ; Lyllana ; Minivelle ; Vivelledot	Estradiol TD Patch Twice Weekly 0.0375 MG/24HR	0.0375 MG/24HR	8	Patches	28	DAYS			
Elestrin	Estradiol Gel 0.06% (0.52 MG/0.87 GM Metered-Dose Pump)	0.06 %	1	Pump	30	DAYS			
Estrace	Estradiol Vaginal Cream 0.1 MG/GM	0.1 MG/GM	6	Tubes	365	DAYS			
Estring	Estradiol Vaginal Ring 2 MG (7.5 MCG/24HRS)	2 MG ; 7.5 MCG/24 HR	1	Ring	90	DAYS			
Estrogel	Estradiol Gel 0.06% (0.75 MG/1.25 GM Metered-Dose Pump)	0.06 %	1	Pump	30	DAYS			
Evamist	Estradiol Transdermal Spray 1.53 MG/SPRAY	1.53 MG/SPRAY	5	Vials	93	DAYS			
Femring	Estradiol Acetate Vaginal Ring 0.05 MG/24HR	0.05 MG/24HR	1	Ring	90	DAYS			
Femring	Estradiol Acetate Vaginal Ring 0.1 MG/24HR	0.1 MG/24HR	1	Ring	90	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Imvexxy maintenance pack	Estradiol Vaginal Insert 10 MCG	10 MCG	8	Units	28	DAYS			
Imvexxy maintenance pack	Estradiol Vaginal Insert 4 MCG	4 MCG	8	Units	28	DAYS			
Imvexxy starter pack	Estradiol Vaginal Insert Starter Pack 10 MCG	10 MCG	18	Units	180	DAYS			
Imvexxy starter pack	Estradiol Vaginal Insert Starter Pack 4 MCG	4 MCG	18	Units	180	DAYS			
Menostar	Estradiol TD Patch Weekly 14 MCG/24HR	14 MCG/24 HR	4	Patches	28	DAYS			

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.025 MG/24HR	0.025 MG/24HR	Medicaid
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.05 MG/24HR	0.05 MG/24HR	Medicaid
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.075 MG/24HR	0.075 MG/24HR	Medicaid
Alora ; Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.1 MG/24HR	0.1 MG/24HR	Medicaid
Climara	Estradiol TD Patch Weekly 0.025 MG/24HR	0.025 MG/24HR	Medicaid
Climara	Estradiol TD Patch Weekly 0.0375 MG/24HR (37.5 MCG/24HR)	37.5 MCG/24HR	Medicaid
Climara	Estradiol TD Patch Weekly 0.05 MG/24HR	0.05 MG/24HR	Medicaid
Climara	Estradiol TD Patch Weekly 0.06 MG/24HR	0.06 MG/24HR	Medicaid
Climara	Estradiol TD Patch Weekly 0.075 MG/24HR	0.075 MG/24HR	Medicaid
Climara	Estradiol TD Patch Weekly 0.1 MG/24HR	0.1 MG/24HR	Medicaid
Climara pro	Estradiol-Levonorgestrel TD Patch Weekly 0.045-0.015 MG/DAY	0.045-0.015 MG/DAY	Medicaid
Combipatch	Estradiol-Norethindrone Ace TD PTTW 0.05-0.14 MG/DAY	0.05-0.14 MG/DAY	Medicaid
Combipatch	Estradiol-Norethindrone Ace TD PTTW 0.05-0.25 MG/DAY	0.05-0.25 MG/DAY	Medicaid
Divigel	Estradiol TD Gel 0.25 MG/0.25GM (0.1%)	0.25 MG/0.25GM	Medicaid
Divigel	Estradiol TD Gel 0.5 MG/0.5GM (0.1%)	0.5 MG/0.5GM	Medicaid
Divigel	Estradiol TD Gel 0.75 MG/0.75GM (0.1%)	0.75 MG/0.75GM	Medicaid
Divigel	Estradiol TD Gel 1 MG/GM (0.1%)	1 MG/GM	Medicaid
Divigel	Estradiol TD Gel 1.25 MG/1.25GM (0.1%)	1.25 MG/1.25GM	Medicaid
Dotti ; Lyllana ; Minivelle ; Vivelle-dot	Estradiol TD Patch Twice Weekly 0.0375 MG/24HR	0.0375 MG/24HR	Medicaid
Elestrin	Estradiol Gel 0.06% (0.52 MG/0.87 GM Metered-Dose Pump)	0.06 %	Medicaid
Estrace	Estradiol Vaginal Cream 0.1 MG/GM	0.1 MG/GM	Medicaid
Estring	Estradiol Vaginal Ring 2 MG (7.5 MCG/24HRS)	2 MG ; 7.5 MCG/24HR	Medicaid
EstroGel	Estradiol Gel 0.06% (0.75 MG/1.25 GM Metered-Dose Pump)	0.06 %	Medicaid

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Evamist	Estradiol Transdermal Spray 1.53 MG/SPRAY	1.53 MG/SPRAY	Medicaid
Femring	Estradiol Acetate Vaginal Ring 0.05 MG/24HR	0.05 MG/24HR	Medicaid
Femring	Estradiol Acetate Vaginal Ring 0.1 MG/24HR	0.1 MG/24HR	Medicaid
Imvexxy maintenance pack	Estradiol Vaginal Insert 10 MCG	10 MCG	Medicaid
Imvexxy maintenance pack	Estradiol Vaginal Insert 4 MCG	4 MCG	Medicaid
Imvexxy starter pack	Estradiol Vaginal Insert Starter Pack 10 MCG	10 MCG	Medicaid
Imvexxy starter pack	Estradiol Vaginal Insert Starter Pack 4 MCG	4 MCG	Medicaid
Menostar	Estradiol TD Patch Weekly 14 MCG/24HR	14 MCG/24HR	Medicaid

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	<p>Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met:</p> <ol style="list-style-type: none"> 1. The requested quantity (dose) does NOT exceed the program quantity limit OR 2. The requested quantity (dose) is greater than the program quantity limit AND ONE of the following: <ol style="list-style-type: none"> A. BOTH of the following: <ol style="list-style-type: none"> 1. The patient has a diagnosis of gender dysphoria/gender incongruent AND 2. The requested agent is ONE of the following: <ol style="list-style-type: none"> A. Alora (estradiol) B. Climara (estradiol) C. Divigel (estradiol) D. Elestrin (estradiol) E. Estrogel (estradiol) F. EvaMist (estradiol) G. Menostar (estradiol) H. Minivelle (estradiol) I. Vivelle Dot (estradiol) OR B. BOTH of the following: <ol style="list-style-type: none"> 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication AND 2. Information has been provided to support therapy with a higher dose for the requested indication OR C. BOTH of the following: <ol style="list-style-type: none"> 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication AND 2. Information has been provided to support why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit OR D. BOTH of the following: <ol style="list-style-type: none"> 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication AND 2. Information has been provided to support therapy with a higher dose for the requested indication <p>Length of Approval: up to 12 months</p>

