



## Drug Quantity Management – Per Days Estrogens (Topical) – Patches

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### Product Identifier(s)

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### National Formulary Medical Necessity

#### Drugs Affected

- Alora® (estradiol transdermal system [patch])
- Climara® (estradiol transdermal system [patch] – generic)
- Menostar® (estradiol transdermal system [patch])
- Minivelle™ (estradiol transdermal system [patch] – generic, Lyllana™)
- Vivelle-Dot® (estradiol transdermal system [patch] – generic, Dotti™)

This Drug Quantity Management program has been developed to prevent the stockpiling, misuse, and/or overuse of the estrogen patch products. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. Note: Combination estrogen patches (e.g., Climara Pro® [estradiol/levonorgestrel transdermal system]) are subject to quantity limits, but are not included in this policy as they do not have override criteria. Approvals are provided for 1 year in duration, unless otherwise noted below.

### Drug Quantity Limits

Product	Strengths (mg/24 hour)	Maximum Quantity per 28 Days*
Alora® (estradiol transdermal system)	0.025, 0.05, 0.075, 0.1 Boxes of 8 patches	8 patches
Climara® (estradiol transdermal system, generic)	0.025, 0.0375, 0.05, 0.06, 0.075, 0.1 Boxes of 4 patches	4 patches
Menostar® (estradiol transdermal system)	0.014 Boxes of 4 patches	4 patches
Minivelle™ (estradiol transdermal system, generic, including Lyllana™)	0.025, 0.0375, 0.05, 0.075, 0.1 Boxes of 8 patches	8 patches
Vivelle-Dot® (estradiol transdermal system, generic, including Dotti™)	0.025 (generic only), 0.0375, 0.05, 0.075, 0.1 Boxes of 8 patches	8 patches

\* The quantity limit accumulates (is combined) for weekly patches and semiweekly patches.

### Criteria

#### Cigna covers quantities as medically necessary when the following criteria are met:

##### Climara 0.025 mg/24 hr, 0.0375 mg/24 hr, 0.05 mg/24 hr, and 0.06 mg/24 hr transdermal patches (generic)

1. If the individual is changing strengths to another once-weekly patch within the same month, approve a one-time override for 4 additional patches.
2. If the individual is using the patch in a protocol for Assisted Reproductive Technology procedures (e.g., *in vitro* fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer) AND infertility is a covered benefit, approve the quantity requested for 1 year.

##### Climara 0.075 mg/24 hr transdermal patch (generic)

1. If the individual is changing strengths to another once-weekly patch within the same month, approve a one-time override for 4 additional patches.
2. If the individual requires two patches to be applied simultaneously, approve up to 8 patches per 28 days.
3. If the individual is using the patch in a protocol for Assisted Reproductive Technology procedures (e.g., *in vitro* fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer) AND infertility is a covered benefit, approve the quantity requested for 1 year.

##### Climara 0.1 mg/24 hr transdermal patch (generic)

1. If the individual is changing strengths to another once-weekly patch within the same month, approve a one-time override for 4 additional patches.
2. If the individual requires two patches to be applied simultaneously, approve up to 8 patches per 28 days.
3. If the individual is using the patch in a protocol for Assisted Reproductive Technology procedures (e.g., *in vitro* fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer) AND infertility is a covered benefit, approve the quantity requested for 1 year.

##### Menostar 0.014 mg/24 hr transdermal patch

1. If the individual is changing strengths to another once-weekly patch within the same month, approve a one-time override for 4 additional patches.

##### Alora 0.025 mg/24 hr and 0.05 mg/24 hr transdermal patches; Minivelle 0.025 mg/24 hr, 0.0375 mg/24 hr, and 0.05 mg/24 hr transdermal patches (generic); Vivelle-Dot 0.025 mg/24 hr, 0.0375 mg/24 hr, and 0.05 mg/24 hr transdermal patches (generic)

1. If the individual is changing strengths to another twice-weekly patch within the same month, approve a one-time override for 8 additional patches.

- If the individual is using the patch in a protocol for Assisted Reproductive Technology procedures (e.g., *in vitro* fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer) AND infertility is a covered benefit, approve the quantity requested for 1 year.

Alora 0.075 mg/24 hr transdermal patch, Minivelle 0.075 mg/24 hr transdermal patch (generic), Vivelle-Dot 0.075 mg/24 hr transdermal patch (generic)

- If the individual is changing strengths to another twice-weekly patch within the same month, approve a one-time override for 8 additional patches.
- If the individual requires two patches to be applied simultaneously, approve up to 16 patches per 28 days.
- If the individual is using the patch in a protocol for Assisted Reproductive Technology procedures (e.g., *in vitro* fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer) AND infertility is a covered benefit, approve the quantity requested for 1 year.

Alora 0.1 mg/24 hr transdermal patch, Minivelle 0.1 mg/24 hr transdermal patch (generic), Vivelle-Dot 0.1 mg/24 hr transdermal patch (generic)

- If the individual is changing strengths to another twice-weekly patch within the same month, approve a one-time override for 8 additional patches.
- If the individual requires two patches to be applied simultaneously, approve up to 16 patches per 28 days.
- If the individual is using the patch in a protocol for Assisted Reproductive Technology procedures (e.g., *in vitro* fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer) AND infertility is a covered benefit, approve the quantity requested for 1 year.
- If the individual is a gender-dysphoric/gender-incongruent person or a person undergoing male-to-female gender reassignment, approve up to 32 patches per 28 days.

## Conditions Not Covered

Any other exception is considered not medically necessary.

## Background

### Overview

Alora, Climara (generic), and Vivelle-Dot (generic) are indicated for the **prevention of postmenopausal osteoporosis; treatment of moderate or severe vasomotor symptoms associated with menopause, moderate or severe vulvar/vaginal atrophy associated with menopause, and hypoestrogenism due to hypogonadism, castration (ovariectomy), or primary ovarian failure.**<sup>1,3,5,6</sup> Minivelle (generic) is indicated for the treatment of **moderate to severe vasomotor symptoms due to menopause and prevention of postmenopausal osteoporosis.**<sup>4</sup> Menostar is the only estrogen patch product with the single indication for **prevention of postmenopausal osteoporosis.**<sup>2</sup>

### Dosing and Availability

**Table 1. Strength and Dosing for Estrogen Patches.**<sup>1-6</sup>

	Strengths Available (mg/24 hour)	Dosing Frequency
Alora <sup>®</sup> (estradiol transdermal system)	0.025, 0.05, 0.075, 0.1 Boxes of 8 patches	Twice weekly
Climara <sup>®</sup> (estradiol transdermal system, generic)	0.025, 0.0375, 0.05, 0.06, 0.075, 0.1 Boxes of 4 patches	Once weekly
Menostar <sup>®</sup> (estradiol transdermal system)	0.014 Boxes of 4 patches	Once weekly
Minivelle <sup>™</sup> (estradiol transdermal system, generic, including Lyllana <sup>™</sup> )	0.025, 0.0375, 0.05, 0.075, 0.1 Boxes of 8 patches	Twice weekly
Vivelle-Dot <sup>®</sup> (estradiol transdermal system, generic, including Dotti <sup>™</sup> )	0.025 (generic only), 0.0375, 0.05, 0.075, 0.1 Boxes of 8 patches	Twice weekly

## Off-Label Uses

Estrogens have been used off-label in protocols for **Assisted Reproductive Technology** procedures.<sup>7</sup> In these protocols, estrogens are used to prepare the endometrium, usually at higher doses than are used for labeled indications. Generally, transdermal estrogens are preferred over oral estrogens due to the bypass of the first-pass metabolism by the liver. This allows administration of estrogen at lower doses to possibly reduce the risk of adverse events.

Estrogens are also used off-label for hormone replacement in **gender-dysphoria/gender-incongruent persons and persons undergoing male-to-female gender reassignment**.<sup>8</sup> Guidelines from the Endocrine Society (2017) note that transdermal estradiol patches can be used, with a new patch placed every 3 to 5 days. The guideline-recommended dose of estradiol transdermal patches ranges from 0.025 to 0.2 mg/day.

## References

1. Climara® transdermal system [prescribing information] Whippany, NJ: Bayer HealthCare; September 2021.
2. Menostar® transdermal system [prescribing information]. Whippany, NJ: Bayer HealthCare; September 2021.
3. Alora® transdermal system [prescribing information]. Madison, NJ: Allergan USA; March 2020.
4. Minivelle® transdermal system [prescribing information]. Miami, FL: Noven; October 2021.
5. Vivelle-Dot® transdermal system [prescribing information]. East Hanover, NJ: Novartis; October 2021.
6. Estradiol transdermal system (twice-weekly) [prescribing information]. Morgantown, WV: Mylan; October 2021.
7. Vartanyan E, Tsaturova K, Devyatova E. Thin endometrium problem in IVF programs. *Gynecol Endocrinol.* 2020;36(sup 1):24-27.
8. 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(11): 3869-3903.

## Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	<ul style="list-style-type: none"><li>• Approval duration was changed from 3 years to 1 year.</li><li>• Clarified override criteria that one-time overrides are for a specific one-time quantity, not an ongoing quantity per 28 days.</li><li>• Updated wording related to gender reassignment: Added gender-dysphoric/gender-incongruent person wording to applicable criteria.</li><li>• Removed Exception prohibiting more frequent patch application. Specific override criteria to address these scenarios are provided.</li><li>• Named generics, Lyllana and Dotti added to the policy.</li></ul>	04/13/2022

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