

## **Clinical Policy: Doxepin (Silenor, Prudoxin, Zonalon)**

Reference Number: HIM.PA.147

Effective Date: 11.17.17

Last Review Date: 11.24

Line of Business: HIM

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Doxepin (Silenor<sup>®</sup>, Prudoxin<sup>™</sup>, Zonalon<sup>®</sup>) is a tricyclic antidepressant.

### **FDA Approved Indication(s)**

Silenor is indicated for treatment of insomnia characterized by difficulties with sleep maintenance.

Prudoxin and Zonalon are indicated for the short-term (up to 8 days) management of moderate pruritus in adult patients with atopic dermatitis or lichen simplex chronicus.

### **Policy/Criteria**

*Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Silenor, Prudoxin, and Zonalon are **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

##### **A. Insomnia (must meet all):**

1. Diagnosis of insomnia;
2. Request is for doxepin tablets (Silenor);
3. Age  $\geq$  18 years;
4. Failure of two preferred or formulary agents indicated for insomnia (*see Appendix B for examples*) at maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
5. For brand Silenor requests, member must use doxepin tablets (generic Silenor), unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 6 mg (1 tablet) per day.

**Approval duration: 6 months**

##### **B. Pruritus (must meet all):**

1. Diagnosis of pruritus associated with conditions such as atopic dermatitis (eczema) or lichen simplex chronicus\*;
2. Request is for doxepin cream (Prudoxin, Zonalon);
3. Age  $\geq$  18 years;

4. Failure of  $\geq 2$  topical therapies (*see Appendix B for examples*) in the last 6 months, unless clinically significant adverse effects are experienced or all are contraindicated (if appropriate, at least one trial should include a topical corticosteroid);
5. For brand Prudoxin or Zonalon requests, member must use generic doxepin cream, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed topical application up to four times daily.

**Approval duration: 6 months (1 tube)**

*\*Lichen simplex chronicus is a secondary skin condition resulting from excessive scratching associated with a variety of conditions including atopic dermatitis. Complaints of intense pruritus are common.*

**C. Other diagnoses/indications (must meet 1 or 2):**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

**II. Continued Therapy**

**A. Insomnia (must meet all):**

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Request is for doxepin tablets (Silenor);
3. Member is responding positively to therapy;
4. For brand Silenor requests, member must use doxepin tablets (generic Silenor), unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, new dose does not exceed 6 mg (1 tablet) per day.

**Approval duration: 12 months**

**B. Pruritus (must meet all):**

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

- b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
- 2. Request is for doxepin cream (Prudoxin, Zonalon);
- 3. Member is responding positively to therapy;
- 4. For brand Prudoxin or Zonalon requests, member must use generic doxepin cream, unless contraindicated or clinically significant adverse effects are experienced;
- 5. Member has not received topical doxepin in the last 180 days;
- 6. If request is for a dose increase, new dose does not exceed topical application up to four times daily.

**Approval duration: 6 months (1 tube)**

**C. Other diagnoses/indications (must meet 1 or 2):**

- 1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
- 2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug Name                           | Dosing Regimen  | Dose Limit/<br>Maximum Dose           |
|-------------------------------------|---|---------------------------------------|
| <b>Insomnia</b>                     |   |                                       |
| estazolam                           | 1 mg PO HS PRN  | 2 mg/day                              |
| eszopiclone (Lunesta <sup>®</sup> ) | Adults: 1 mg – 3 mg PO HS PRN<br>Elderly: 1 mg - 2 mg PO HS PRN | Adults: 3 mg/day<br>Elderly: 2 mg/day |

| Drug Name   | Dosing Regimen   | Dose Limit/<br>Maximum Dose |
|---|--|-----------------------------|
| ramelteon (Rozerem <sup>®</sup> )   | Adults: 8 mg PO HS PRN   | 8 mg/day                    |
| temazepam (Restoril <sup>®</sup> )  | Adults: 15 – 30 mg PO HS PRN<br>Elderly: 7.5 – 15 mg PO HS PRN             | 30 mg/day                   |
| triazolam (Halcion <sup>®</sup> )   | 0.25 mg PO HS PRN  | 0.5 mg/day                  |
| zaleplon (Sonata <sup>®</sup> )   | 10 mg PO HS PRN  | 20 mg/day                   |
| zolpidem CR (Ambien CR <sup>®</sup> )   | Adults: 6.25-12.5 mg PO HS PRN<br>Elderly: 6.25 mg PO HS PRN               | 12.5 mg/day                 |
| zolpidem IR (Ambien <sup>®</sup> )  | 5 mg PO HS PRN   | 10 mg/day                   |
| <b>Pruritis</b>   |  |                             |
| clobetasol propionate, 0.05%  | Topical application up to two times daily                                  | Varies                      |
| desonide, 0.05%   | Topical application up to two to four times daily depending on formulation |                             |
| halcinonide, 0.1% (Halog <sup>®</sup> )   | Topical application up to three times daily                                |                             |
| OTC topical diphenhydramine 1-2% (e.g., Anti-Itch <sup>®</sup> Maximum Strength, Anti-Itch <sup>®</sup> , Benadryl <sup>®</sup> Itch Stopping, Itch Relief <sup>®</sup> ) | Topical application up to four times daily                                 |                             |

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

#### Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Individuals who have shown hypersensitivity to doxepin HCl, any of its inactive ingredients, or other dibenzoxepines
  - Concomitant use with monoamine oxidase inhibitors (MAOIs) (*Silenor only*)
  - Patients with untreated narrow angle glaucoma or severe urinary retention
- Boxed warning(s): none reported

#### V. Dosage and Administration

| Drug Name                   | Indication        | Dosing Regimen  | Maximum Dose     |
|-----------------------------|-------------------|---|------------------|
| Doxepin (Silenor)           | Insomnia          | Adults: 6 mg PO HS PRN<br>Elderly: 3 mg PO HS PRN   | 6 mg/day         |
| Doxepin (Prudoxin, Zonalon) | Moderate pruritus | Apply to the affected area(s) topically 4 times daily allowing at least 3 to 4 hours between applications, for up to 8 days | For up to 8 days |

#### VI. Product Availability

| Drug Name         | Product Availability |
|-------------------|----------------------|
| Doxepin (Silenor) | Tablets: 3 mg, 6 mg  |

| Drug Name          | Product Availability  |
|--------------------|-----------------------|
| Doxepin (Prudoxin) | Cream, 5%: 45 g       |
| Doxepin (Zonalon)  | Cream, 5%: 30 g, 45 g |

**VII. References**

1. Prudoxin Prescribing Information. Morgantown, WV: Mylan Pharmaceuticals, Inc.; June 2017. Available at <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=ca53346b-8ab3-4722-98f6-cf272706d3fa>. Accessed July 11, 2024.
2. Zonalon Prescribing Information. Morgantown, WV: Mylan Pharmaceuticals, Inc.; June 2017. Available at <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5f302247-525e-4acc-852b-00eb1d79af4b>. Accessed July 11, 2024.
3. Clinical Pharmacology [database online]. Elsevier, Inc.; 2022. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed July 26, 2024.
4. Patel T, Yosipovitch G. Therapy of pruritis. Expert Opin Pharmacother. 2010; 11(10): 1673-1682.
5. Silenor Prescribing Information. Morristown, NJ: Pernix Therapeutics, LLC, Inc.; December 2022. Available at: <https://www.silenor.com/wp-content/themes/Silenor/pdf/SIL-LC087-02%20PI.pdf>. Accessed July 12, 2024.
6. Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(2):307–349.

| Reviews, Revisions, and Approvals   | Date     | P&T Approval Date |
|---|----------|-------------------|
| 4Q 2020 annual review: no significant changes; added product specification for each diagnosis in Section II; references reviewed and updated.   | 08.21.20 | 11.20             |
| 4Q 2021 annual review: no significant changes; revised reference from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.   | 07.21.21 | 11.21             |
| 4Q 2022 annual review: added requirement for use of generic product for brand requests; clarified that criteria also applies to generic requests; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section. | 07.05.22 | 11.22             |
| 4Q 2023 annual review: no significant changes; references reviewed and updated.   | 07.12.23 | 11.23             |
| 4Q 2024 annual review: no significant changes; references reviewed and updated.   | 07.11.24 | 11.24             |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional

organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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