Clinical Policy: Doxepin (Silenor, Prudoxin, Zonalon)

Reference Number: HIM.PA.147
Effective Date: 11.17.17
Last Review Date: 11.22
Line of Business: HIM

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Doxepin (Silenor®, Prudoxin™, Zonalon®) 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® 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 ≥ 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 ≥ 18 years;

4. Failure of ≥ 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/ Maximum Dose
Insomnia		
estazolam	1 mg PO HS PRN	2 mg/day
eszopiclone (Lunesta®)	Adults: 1 mg – 3 mg PO HS PRN Elderly: 1 mg - 2 mg PO HS PRN	Adults: 3 mg/day Elderly: 2 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ramelteon (Rozerem®)	Adults: 8 mg PO HS PRN	8 mg/day
temazepam (Restoril®)	Adults: 15 – 30 mg PO HS PRN Elderly: 7.5 – 15 mg PO HS PRN	30 mg/day
triazolam (Halcion®)	0.25 mg PO HS PRN	0.5 mg/day
zaleplon (Sonata®)	10 mg PO HS PRN	20 mg/day
zolpidem CR (Ambien CR®)	Adults: 6.25-12.5 mg PO HS PRN Elderly: 6.25 mg PO HS PRN	12.5 mg/day
zolpidem IR (Ambien®)	5 mg PO HS PRN	10 mg/day
Pruritis		
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®)	Topical application up to three times daily	
OTC topical diphenhydramine 1-2% (e.g., Anti-Itch® Maximum Strength, Anti-Itch®, Benadryl® Itch Stopping, Itch Relief®)	Topical application up to four times daily	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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 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 5, 2022.
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 5, 2022.
3. Clinical Pharmacology [database online]. Elsevier, Inc.; 2022. Available at: https://www.clinicalkey.com/pharmacology/. Accessed July 5, 2022.
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.; October 2020. Available at: https://www.silenor.com. Accessed July 5, 2022.
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
1Q 2019 annual review: no significant changes; references reviewed and updated.	12.07.18	02.19
4Q 2019 annual review: added Silenor and criteria for insomnia; references reviewed and updated.	08.27.19	11.19
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

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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.