Clinical Policy: Minocycline ER (Solodyn, Ximino) and Microspheres (Arestin)

Reference Number: CP.PMN.80
Effective Date: 05.01.17
Last Review Date: 05.18
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Minocycline ER [extended release] (Solodyn®, Ximino™) and microspheres (Arestin®) are tetracycline-class drugs.

FDA Approved Indication(s)

Solodyn and Ximino are indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Solodyn and Ximino should be used only as indicated.

- Limitation(s) of use: Solodyn and Ximino did not demonstrate any effect on non-inflammatory acne lesions. Safety of these drugs have not been established beyond 12 weeks of use. This formulation of minocycline has not been evaluated in the treatment of infections.

Arestin is indicated as an adjunct to scaling and root planing procedures for reduction of pocket depth in patients with adult periodontitis. Arestin may be used as part of a periodontal maintenance program which includes good oral hygiene and scaling and root planing.

Policy/Criteria

Provider must submit documentation (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 Solodyn and Arestin are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acne Vulgaris (must meet all)**:**

1. Diagnosis of acne vulgaris;
2. Request is for Solodyn or Ximino;
3. Age ≥ 12 years;
4. Medical justification supports inability to use immediate-release minocycline (e.g., member experienced clinically significant adverse effects or has contraindication(s) to the excipients in immediate-release minocycline);
5. Failure of a ≥ 4 week trial of one additional preferred oral tetracycline antibiotic (e.g., immediate-release doxycycline) unless clinically significant adverse effects are experienced;

6. Dose does not exceed 135 mg/day.

Approval duration: 12 weeks

B. Periodontitis (must meet all)**:**
1. Diagnosis of chronic periodontitis (also known as adult periodontitis);
2. Request is for Arestin;
3. Prescribed by or in consultation with a periodontist;
4. Age ≥ 18 years;
5. Intolerance or contraindication to oral doxycycline hyclate at a sub-antimicrobial dose (20 mg PO twice a day) (e.g., unable to swallow capsules, allergic to a doxycycline product excipient, history of gastrointestinal disease);
6. Prescribed as an adjunct to a scaling and root planing procedure to reduce pocket depth (applied during procedure);
7. Dose is individualized depending on the size, shape, and number of pockets being treated.

Approval duration: 1 procedure

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acne Vulgaris (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Solodyn or Ximino;
3. One of the following (a or b):
   a. Member has not completed current 12-week course of treatment with Solodyn/Ximino and is responding positively to therapy;
   b. At least 12 months have elapsed since the last treatment course;
4. If request is for a dose increase, new dose does not exceed 135 mg/day.

Approval duration: up to 12 weeks of total treatment/365 days

B. Periodontitis (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Arestin;
3. Member has not received 4 scaling and root planing procedures in the last 365 days;
4. Dose is individualized depending on the size, shape, and number of pockets being treated.

Approval duration: 1 procedure

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 weeks (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid 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
doxycycline (Vibramycin®)	Acne Vulgaris Adults, adolescents, and children 8 years and older weighing 45 kg or more: 100 mg PO every 12 hours on day 1, then 100 mg PO once daily Children 8 years and older and adolescents weighing less than 45 kg: 2.2 mg/kg/dose PO every 12 hours on day 1, then 2.2 mg/kg/dose PO once daily	Varies
minocycline (Minocin®)	Acne Vulgaris Adults: 200 mg PO initially, then 100 mg PO every 12 hours as adjunctive therapy. Alternatively, if more frequent oral doses are preferred, 100 to 200 mg PO initially, then 50 mg PO every 6 hours Children ≥ 8 years and adolescents: 4 mg/kg PO (max: 200 mg) initially, then 2 mg/kg/dose PO every 12 hours (max: 100 mg/dose) as adjunctive therapy	200 mg/day
tetracycline	Acne Vulgaris Adults: 1 g/day PO in divided doses, then decrease slowly to 125 to 500 mg PO daily or every other day Children ≥ 9 years and adolescents: 1 g/day PO in divided doses, then decrease	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	slowly to 125 to 500 mg PO daily or every other day	
doxycycline (Periostat®)	Periodontitis 20 mg BID (subantimicrobial-dose) for 3 to 9 months	40 mg/day

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: General Information

- Arestin is a variable dose product, dependent on the size, shape, and number of pockets being treated. In US clinical trials, up to 122 unit-dose cartridges were used in a single visit and up to 3 treatments, at 3-month intervals, were administered in pockets with pocket depth of 5 mm or greater.
- The 2015 American Dental Association guidelines rank the following drug therapies as adjuncts to scaling and root planing for chronic periodontitis (rankings in order of strength are 1) strong, 2) in favor, 3) weak, 4) expert opinion for, 5) expert opinion against, 6) against):
  - "In favor":
    - Systemic subantimicrobial-dose doxycycline
  - "Weak":
    - Systemic antimicrobials at standard doses (similar benefit to subantimicrobial doses but increased risk of adverse effects)
    - Chlorhexidine chips (locally applied)
    - Photodynamic therapy with diode laser
  - "Expert opinion for"
    - Doxycycline hyclate gel (locally applied)
    - Minocycline microspheres (locally applied)

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Minocycline extended release tablets (Solodyn)	Acne vulgaris	The recommended dosage is approximately 1 mg/kg PO once daily for 12 weeks. The following table shows tablet strength and body weight to achieve approximately 1 mg/kg:	1 mg/kg/day PO up to 135 mg/day PO

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><th>Wt. (lbs)</th><th>Wt. (kg)</th><th>Tablet Strength (mg)</th><th>Actual mg/kg dose</th></tr>
<tr><td>99-109</td><td>45-49</td><td>45</td><td>1-0.92</td></tr>
<tr><td>110-131</td><td>50-59</td><td>55</td><td>1.10-0.93</td></tr>
<tr><td>132-157</td><td>60-71</td><td>65</td><td>1.08-0.92</td></tr>
<tr><td>158-186</td><td>72-84</td><td>80</td><td>1.11-0.95</td></tr>
<tr><td>187-212</td><td>85-96</td><td>90</td><td>1.06-0.94</td></tr>
<tr><td>213-243</td><td>97-110</td><td>105</td><td>1.08-0.95</td></tr>
<tr><td>244-276</td><td>111-125</td><td>115</td><td>1.04-0.92</td></tr>
<tr><td>277-300</td><td>126-136</td><td>135</td><td>1.07-0.99</td></tr>
</table>
</td><td></td></tr>
<tr><td>Minocycline extended release capsules (Ximino)</td><td>Acne vulgaris</td><td>The recommended dosage is approximately 1 mg/kg PO once daily for 12 weeks. The following table shows capsule strength and body weight to achieve approximately 1 mg/kg:
<table>
<tr><th>Wt. (lbs)</th><th>Wt. (kg)</th><th>Capsule Strength (mg)</th><th>Actual mg/kg dose</th></tr>
<tr><td>99-131</td><td>45-59</td><td>45</td><td>1-0.76</td></tr>
<tr><td>132-199</td><td>60-90</td><td>90</td><td>1.5-1</td></tr>
<tr><td>200-300</td><td>91-136</td><td>135</td><td>1.48-0.99</td></tr>
</table>
</td><td></td></tr>
<tr><td>Minocycline microspheres (Arestin)</td><td>Periodontitis</td><td>Arestin is a variable dose product, dependent on the size, shape, and number of pockets being treated. In US clinical trials, up to 122 unit-dose cartridges were used in a single visit and up to 3 treatments, at 3-month intervals, were administered in pockets with pocket depth of 5 mm or greater.

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Arestin is provided as a dry powder, packaged in a unit-dose cartridge with a deformable tip, which is inserted into a</td><td>Dose is variable depending on size, shape, and number of pockets being treated.</td></tr>
</table>

Drug Name	Indication	Dosing Regimen	Maximum Dose
		spring-loaded cartridge handle mechanism to administer the product. *The oral health care professional removes the disposable cartridge from its pouch and connects the cartridge to the handle mechanism.*	

VI. Product Availability

Drug Name	Availability
Minocycline extended release tablets (Solodyn)	Extended-release tablets: 45 mg†, 55 mg, 65 mg, 80 mg, 90 mg†, 105 mg, 115 mg, and 135 mg†
Minocycline extended release capsules (Ximino)	Extended-release capsules: 45 mg, 90 mg, and 135 mg
Minocycline microspheres (Arestin)	Unit-dose cartridge: minocycline hydrochloride microspheres equivalent to 1 mg of minocycline free base (1 or 12 unit-dose cartridges per box)

†*available as generic only*

VII. References

1. Solodyn Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; September 2017. Available at: http://www.solodyn.com/. Accessed January 29, 2018.
2. Minocycline Extended Release Tablets Prescribing Information. Baltimore, MD: Lupin Pharmaceuticals, Inc.; June 2016. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed September 20, 2017.
3. Ximino Prescribing Information. New Brunswick, NJ: Ohm Laboratories Inc.; April 2017. Available at: http://www.ximinorx.com/. Accessed June 1, 2018.
4. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016; 74(5):945-973.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.
6. Arestin Prescribing Information. Bridgewater, NJ: OraPharma, a division of Valeant Pharmaceuticals North America LLC. May 2017. Available at http://www.valeant.com/Portals/25/Pdf/PI/arestin-pi.pdf. Accessed January 29, 2018.
7. Smiley CJ, Tracy SL, Abt E, et al. Systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts. July 2015. JADA 146(7): 508-524.e5.
8. Smiley CJ, Tracy SL, Abt E, et al. Evidence-based clinical practice guideline on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts. July 2015. JADA 146(7): 525-535.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PMN.51 Tetracycline Antibiotics (Solodyn, Doryx, Oracea) -Modified criteria related to trial and failure of PDL oral antibiotics to specifically require tetracycline class of antibiotics, one of which must be immediate-release minocycline, as they are considered first-line for systemic antibiotic therapy for acne for ≥ 4 weeks -Converted to new template -Added no documentation of hypersensitivity to tetracyclines per PI -Added duration of trial to requirements related to trial and failure of topical therapies for clarity -Removed age requirement since tetracycline antibiotics on the PDL are not subjected to age restrictions -Updated references	03.17	05.17
2Q 2018 annual review: policies combined for commercial and Medicaid lines of business; added Arestin and criteria for periodontitis Commercial: split from CP.CPA.210 doxycycline hyclate (Acticlate, Doryx), doxycycline (Oracea), and minocycline (Solodyn); acne vulgaris: modified "failure of both generic immediate release minocycline and doxycycline" requirement to the following: "Medical justification supports inability to use immediate-release minocycline (e.g., member experienced clinically significant adverse effects to immediate-release minocycline or has contraindication(s) to the excipients in immediate-release minocycline) and "Failure of a ≥ 4 week trial of one additional preferred oral tetracycline antibiotic (e.g., immediate-release doxycycline) unless clinically significant adverse effects are experienced"; modified initial/continued approval duration from length of benefit to 12 weeks/up to 12 weeks of total treatment/365 days, respectively as safety of Solodyn has not been established beyond 12 weeks of use; Medicaid: Acne vulgaris: added age; removed criteria related to topical treatments and hypersensitivity to tetracyclines; added max dose; specified request is for Solodyn. Re-auth: modified approval duration from "up to 12 weeks of total treatment" to "up to 12 weeks of total treatment/365 days"; references reviewed and updated.	02.06.18	05.18
No significant changes: added Ximino back to the policy as it was unintentionally omitted during 2Q 2018 annual review.	06.20.18	

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.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.