Clinical Policy: Minocycline ER (Solodyn, Ximino) and Microspheres (Arestin)
Reference Number: ERX.NPA.51
Effective Date: 01.11.17
Last Review Date: 05.19

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
derivative antibiotics.

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 Solodyn and Ximino have not been established beyond 12 weeks of use. This
formulation of minocycline has not been evaluated in the treatment of infections. 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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to
use preferred alternative agents apply only when such requirements align with the health plan approved
formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Solodyn, Ximino, 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 contraindicated or clinically significant adverse effects
         are experienced;
      6. Dose does not exceed 135 mg per 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

**A. Acne Vulgaris** (must meet all):
1. Previously received medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Request is for Solodyn or Ximino;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 135 mg per day.

**Approval duration: 12 weeks**

**B. Periodontitis** (must meet all):
1. Request is for Arestin;
2. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 weeks (whichever is less); or**
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 policy – ERX.PA.01 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 and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>doxycycline (Vibramycin®)</td>
<td>Acne Vulgaris</td>
<td>Varies</td>
</tr>
</tbody>
</table>
## Drug Name | Dosing Regimen | Dose Limit/Maximum Dose
---|---|---
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
minocycline (Minocin®) | **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 | 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 slowly to 125 to 500 mg PO daily or every other day | Varies
doxycline (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: Contraindications/Boxed Warnings
- **Contraindication(s):** hypersensitivity to minocycline or any tetracyclines
- **Boxed warning(s):** none reported

### Appendix D: 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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minocycline extended release tablets (Solodyn)</td>
<td>Acne vulgaris</td>
<td>1 mg/kg PO once daily for 12 weeks. The following table shows tablet strength and body weight to achieve approximately 1 mg/kg:</td>
<td>up to 135 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Table: Tablet Strength and Body Weight</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Wt. (lbs)</strong></td>
<td><strong>Wt. (kg)</strong></td>
</tr>
<tr>
<td>99-109</td>
<td>45-49</td>
<td>45</td>
<td>1.0-0.92</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>
<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:</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Table: Capsule Strength and Body Weight</strong></td>
<td></td>
</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>
<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.</td>
<td>variable depending on size, shape, and number of pockets being treated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arestin is provided as a dry powder, packaged in a unit-dose cartridge with a deformable tip, which is inserted into a 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.</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minocycline ER (Solodyn)</td>
<td>Extended-release tablets: 45 mg†, 55 mg, 65 mg, 80 mg, 90 mg†, 105 mg, 115 mg, 135 mg†</td>
</tr>
<tr>
<td>Minocycline ER (Ximino)</td>
<td>Extended-release capsules: 45 mg, 90 mg, 135 mg</td>
</tr>
<tr>
<td>Minocycline microspheres (Arestin)</td>
<td>Unit-dose cartridge: minocycline hydrochloride microspheres equivalent to 1 mg of minocycline free base (1 or 12 unit-dose cartridges per box)</td>
</tr>
</tbody>
</table>

†Available as generic only
VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>4Q17 Annual Review</td>
<td>12.16</td>
<td>01.17</td>
</tr>
<tr>
<td>Converted to new template.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial: Modified &quot;Member has failed both generic immediate-release minocycline and doxycycline, unless intolerant or contraindicated&quot; to the following: &quot;Member experienced clinically significant adverse effects to immediate-release minocycline or has contraindication(s) to the excipients in immediate-release minocycline&quot; and &quot;Failure of ≥ 4 week trial of one additional formulary oral tetracycline antibiotic (e.g., immediate-release doxycycline, tetracycline) unless clinically significant adverse effects are experienced” as tetracycline class of antibiotics are considered first-line for systemic antibiotic therapy for acne.</td>
<td>09.11.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Added weight based max dose (and on re-auth).</td>
<td></td>
<td></td>
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<tr>
<td>Updated approval duration from 3 months to 12 weeks per PI.</td>
<td></td>
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</tr>
<tr>
<td>Age edit not applied since formulary tetracycline antibiotics are not subjected to age restrictions.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-auth: Added a requirement that member has not received Solodyn daily for ≥ 12 weeks of therapy per PI.</td>
<td></td>
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<tr>
<td>Modified to include retreatment as an option if 12 months have elapsed since the last treatment course.</td>
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<tr>
<td>Changed approval duration from 6 months to “up to 12 weeks of total treatment/365 days” as safety of minocycline ER tablets has not been established beyond 12 weeks of use.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arestin added for periodontitis.</td>
<td>09.26.17</td>
<td>11.17</td>
</tr>
<tr>
<td>2Q 2018 annual review: No significant changes. Acne vulgaris: added age requirement as safety and effectiveness in pediatric patients below the age of 12 has not been established; modified weight based max dose to max dose of drug (and on re-auth). References reviewed and updated.</td>
<td>01.29.18</td>
<td>05.18</td>
</tr>
<tr>
<td>To align with the newly approved Seysara policy – for continuation of therapy, removed the limit of one course of therapy per 365 days, leaving</td>
<td>11.13.18</td>
<td>02.19</td>
</tr>
</tbody>
</table>
Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>just an approval duration of 12 weeks. Removed the requirement that the member has waited for one year between treatment courses.</td>
<td></td>
</tr>
<tr>
<td>2Q 2019 annual review: no significant changes; added Ximino back to the policy since it requires PA; references reviewed and updated.</td>
<td>02.25.19 05.19</td>
</tr>
</tbody>
</table>

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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