Clinical Policy Title:	minocycline ER
Policy Number:	RxA.218
Drug(s) Applied:	Solodyn®, Ximino™, Minolira® and microspheres Arestin®
Original Policy Date:	02/7/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Minocycline hydrochloride extended-release (Solodyn®, Ximino™, Minolira®) and minocycline hydrochloride microspheres (Arestin®) are tetracycline-class drugs.

Solodyn®, Ximino™, Minolira® are indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older.

Arestin® is indicated as an adjunct to scaling and root planning 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 planning.

Limitation(s) of use:

- Solodyn®, Ximino™, and Minolira® 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. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Solodyn®, Ximino™, and Minolira® should be used only as indicated.

<table>
<tr><th colspan="4">Dosing Information</th></tr>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>minocycline extended-release tablets (Solodyn®)</td><td>Acne vulgaris</td><td>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:
<table><tr><th>Wt. (lbs)</th><th>Wt. (kg)</th><th>Tablet Strength (mg)</th><th>Actual mg/kg dose</th></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>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></table></td><td>Approximately 1 mg/kg/day PO up to 115 mg/day PO</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. (lb)</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>Approximately 1 mg/kg/day PO up to 135 mg/day PO</td></tr>
<tr><td>minocycline microspheres (Arestin®)</td><td>Periodontitis</td><td>Arestin is a variable dose product, dependent on the size, 544shape, 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.
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>Dose is variable depending on size, shape, and number of pockets being treated</td></tr>
</table>

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>minocycline extended-release tablets (Minolira®)</td><td>Acne vulgaris</td><td>The recommended dosage is approximately 1 mg/kg PO once daily for 12 weeks. The following list shows tablet strength and body weight to achieve approximately 1 mg/kg:
<table>
<tr><th>Wt. (lb)</th><th>Daily dose</th><th>Tablet strength & size to administer (mg)</th><th>Actual dose (mg/Kg)</th></tr>
<tr><td>45 - 59</td><td>45-59</td><td>half of 105 mg tablet</td><td>1.16- 0.88</td></tr>
<tr><td>60 – 89</td><td>60-90</td><td>Half of 135 mg tablet</td><td>1.13 - 0.76</td></tr>
<tr><td>90 - 125</td><td></td><td>One 105 mg tablet</td><td>1.17 - 0.84</td></tr>
<tr><td>126 - 136</td><td>91-136</td><td>One 135 mg tablet</td><td>1.07 - 0.99</td></tr>
</table></td><td>Approximately 1 mg/kg/day PO up to 135 mg/day PO</td></tr>
</table>

Dosage Forms

- Minocycline extended- release tablets (Solodyn®): Extended-release tablets: 55 mg, 65 mg, 80 mg, 105 mg, 115 mg
- Minocycline extended- release capsules (Ximino™): Extended-release capsules: 45 mg, 90 mg, and 135 mg
- Minocycline extended- release tablets (Minolira®): Extended-release tablets: 105 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*

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of acne vulgaris;
2. Request is for Solodyn®, Ximino™, or Minolira®;
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 (a or b):
    a. Solodyn®: 115 mg/day
    b. Ximino™ or Minolira®: 135 mg/day

Approval Duration
Commercial: 3 months
Medicaid: 3 months

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
Commercial: 1 procedure
Medicaid: 1 procedure

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Request is for Solodyn®, Ximino™, or Minolira®;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed (a or b):
    a. Solodyn®: 115 mg/day
    b. Ximino™ or Minolira®: 135 mg/day

Approval Duration
Commercial: 3 months
Medicaid: 3 months

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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:
Commercial: 1 procedure
Medicaid: 1 procedure

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

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 slowly to 125 to 500 mg PO daily or every other day	Varies
doxycycline	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 any tetracyclines.

- Boxed Warning(s):
  - None.

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)
- The use of drugs of the tetracycline class during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown).

References

1. Solodyn Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; September 2017. Available at: http://www.solodyn.com/. https://www.bauschhealth.com/Portals/25/Pdf/PI/Solodyn-PI.Pdf Accessed March 15, 2021.
2. Minocycline Extended-Release Tablets Prescribing Information. Baltimore, MD: Lupin Pharmaceuticals, Inc.; December 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=3b1e1cf1-ebd2-4aba-a219-9f9939fdb03b&type=display . Accessed March 15, 2021.
3. Ximino Prescribing Information. Princeton,NJ: Sun Pharmaceuticals; January 2021. Available at: https://www.ximinorx.com/pdf/ximino-er-caps-full-prescribing-information.pdf . Accessed March 04, 2021.
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6. Minolira Prescribing Information. Princeton, NJ: Promius Pharma, LLC.; June 2018. Available at: http://173.203.188.208/live/minolira/wp-content/uploads/2019/03/MinoLira-PI.pdf. Accessed March 10, 2021.
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11. Solodyn available strength. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=050808. Accessed on March 15, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy description table was updated 2. Background information, indications and limitations of use were updated 3. Continuation therapy criteria II.A.1 and II.B.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…" 4. Initial and continuation therapy approval duration was updated to include Medicaid. 5. References were updated.	07/07/2020	09/14/2020
Policy was reviewed: 1. Solodyn 45mg, 90 mg, 135 mg were discontinued strength thus they were removed from the policy. 2. Statement about provider sample, ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 3. Initial Approval criteria I.A.6 and Continued Therapy Approval criteria II.B.4: Maximum dose for Solodyn was updated. 4. Therapeutic alternative verbiage updated to "Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary	03/16/2021	06/10/2021

for preferred agents and utilization management requirements." 5. Periostat was discontinued thus it was removed from Appendix . 6. "The use of drugs of the tetracycline class during tooth development…" was added to Appendix . 7. References were reviewed and updated.		