Clinical Policy Title:	isotretinoin
Policy Number:	RxA.071
Drug(s) Applied:	Claravis™, Absorica®, Absorica LD™, Myorisan®, Zenatane™, Amnesteem®
Original Policy Date:	03/06/2020
Last Review Date:	11/15/2023
Line of Business Policy Applies to:	All lines of business

Background

Isotretinoin (Claravis™, Absorica®, Absorica LD™, Myorisan®, Zenatane™, Amnesteem®) is a retinoid indicated for severe recalcitrant nodular acne in non-pregnant patients 12 years of age and older with multiple inflammatory nodules with a diameter of 5 mm or greater.

Absorica® and Absorica LD™ are not substitutable because of different bioavailability and recommended dosage and they are reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic therapies.

Limitation(s) of use: Claravis™, Absorica®, Absorica LD™, Myorisan®, Zenatane™, and Amnesteem® may only be administered to patients enrolled in the iPLEDGE program.

If a second course of Absorica® and Absorica LD™ therapy is needed, it is not recommended before a two-month waiting period because the patient's acne may continue to improve following a 15 to 20-week course of therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
isotretinoin (Absorica®, Claravis™, Myorisan®, Zenatane™, Amnesteem®)	Severe recalcitrant nodular acne	0.5 to 1 mg/kg/day orally given in two divided doses	2 mg/kg/day
Absorica LD™	Severe recalcitrant nodular acne	0.4 to 0.8 mg/kg/day given in two divided doses	1.6 mg/kg/day

Dosage Forms

- isotretinoin (Absorica®): Capsules: 10 mg, 20 mg, 25 mg, 30 mg, 35 mg, and 40 mg
- isotretinoin (Absorica LD™): Capsules: 8 mg, 16 mg, 20 mg, 24 mg, 28 mg, 32 mg
- isotretinoin (Amnesteem®): Capsules: 10 mg, 20 mg, 40 mg
- isotretinoin (Claravis™, Myorisan®, Zenatane™): Capsules: 10 mg, 20 mg, 30 mg, and 40 mg

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 (must meet all)**:**

1. Diagnosis of severe recalcitrant nodular acne;
2. Age ≥ 12 years;
3. Prescribed by or in consultation with a dermatologist;
4. History of failure, contraindication, or intolerance to an adequate trial of two of the following conventional therapy regimens:
   a. Topical antibiotics (e.g., clindamycin, erythromycin);
   b. Topical anti-infectives (e.g., benzoyl peroxide);
   c. Topical retinoids or retinoid like agents (e.g., tretinoin, adapalene, tazoratene)
   *Prior authorization may be required for tretinoin for age ≥ 30 years.

Approval Duration

All Lines of Business (except Medicare): 12 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication, excluding manufacturer samples;
2. If member has received 20 consecutive weeks of treatment, an 8-week treatment-free interval must be allowed prior to reinitiating isotretinoin treatment;

Approval Duration

All Lines of Business (except Medicare): 12 months

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	Maximum Dose
clindamycin 1% (Cleocin T®, Clindagel®)	Gel, lotion, solution: Apply a thin film (1%) twice daily	Not applicable
erythromycin 2% (Erygel®)	Gel, solution: Apply to the affected area twice daily	Not applicable
sulfacetamide (Klaron®)	Gel, solution: Apply to the affected area twice daily	Not applicable
benzoyl peroxide liquid, gel and lotion	Liquid, gel, and lotion: Apply once daily to four times daily	Not applicable
tretinoin (Retin-A®)	0.025% gel, 0.05% cream, 0.1% cream: Apply once daily	Not applicable

Drug Name	Dosing Regimen	Maximum Dose
doxycycline (Monodox®)	50 to 100 mg orally daily	300 mg per day
erythromycin (EES®, Erythromycin Base®, Ery- Tab®)	250 to 500 mg orally twice daily, followed by twice daily dosing	4 gm per day
minocycline (Minocin®, Solodyn®)	IR: 100 mg orally twice daily ER: 1 mg/kg orally daily	200 mg per day
tetracycline	125 to 250 mg orally every 6 hours for 2 weeks, then 125 to 500 mg orally daily or every other day	4 gm per day
trimethoprim- sulfamethoxazole (Bactrim®)	As directed by physician	20 mg/kg/day of trimethoprim

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):*
  - Pregnancy (category X);
  - Hypersensitivity to the medication or any of its components.

  * Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - If pregnancy occurs during isotretinoin use, there is an extremely high risk for severe birth defects (iPLEDGE REMS program enrolment is required for prescribers, patients, pharmacies, and distributors).

APPENDIX D: General Information

- Micromedex classifies the use of isotretinoin for the non-FDA labeled indication of acne vulgaris as a Class II-a strength of recommendation.
- The American Academy of Dermatology recognizes that isotretinoin is also useful for the management of lesser degrees of acne that are treatment-resistant or for the management of acne that is producing either physical or psychological scarring.
- Micromedex classifies the use of isotretinoin for the non-FDA labeled indication of rosacea as a Class II-a strength of recommendation.
- The American Acne and Rosacea Society Consensus Recommendations recognize that isotretinoin has been shown to be effective in treating some refractory cases of papulopustular rosacea, but therapeutic benefit may require continued use. Due to the limited data on the management of refractory rosacea, isotretinoin should only be considered in select cases.
- Because of the risk of teratogenicity and to minimize fetal exposure, isotretinoin is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called iPLEDGE. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE. Registered and activated pharmacies must receive isotretinoin only from wholesalers registered with iPLEDGE. For more information call 866-495-0654 or visit http://www.ipledgeprogram.com.

References

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3. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, BaLD™win HE, Berson DS, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016 May;74(5):945-973.e33. doi: 10.1016/j.jaad.2015.12.037. Available at: https://sci-hubtw.hkvisa.net/10.1016/j.jaad.2015.12.037. Accessed April 14, 2023.
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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established.	2/2020	03/06/2020
Policy was reviewed: 1. Added dose criteria for initial and continuation of therapy for Absorica® LD™. 2. Added drug information for Absorica LD™ (new formulation). 3. Added dosing regimen, drug availability. 4. Updated background section to include Absorica LD™ Added limitation of use for Absorica®/Absorica LD™	05/2020	05/2020
Policy was reviewed: 1. Clinical policy title table was updated. 2. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 3. Appendix B standard verbiage was updated to "Below are suggested	02/19/2021	03/09/2021

therapeutic alternatives…". Table was also updated to remove discontinued brands Clindamax® and Desquam-X®. 4. References were updated.		
Policy was reviewed: 1. Drugs applied, Background, Dosing information, Dosage forms, Clinical Policy was updated to remove Claravis®, Myorisan®, Zenatane®, Amnesteem® as these drugs no longer require prior authorization. 2. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 3. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 4. Appendix B, Dosing Regimen, Cleocin T, Clindagel: Updated dosing information from Gel, lotion, solution: Apply a thin film twice daily to Gel, lotion, solution Apply a thin film (1%) twice daily for indication acne vulgaris. 5. Appendix B, Maximum Dose, tetracycline: Updated maximum dose information from 4 mg per day to 4 gm per day for indication acne vulgaris. 6. Appendix B, Drug Name: Updated to include new therapeutic alternative Sulfacetamide (Klaron®). 7. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only." 8. Disclaimer about contraindications," Contraindications listed reflect statements made in the	12/07/2021	01/17/2022

manufacturer's package insert.." was added to Appendix C. 9. References were reviewed and updated.		
Policy was reviewed: 1. Drugs applied, Background, Dosing information, Dosage forms, Clinical Policy was updated to include Claravis®, Myorisan®, Zenatane®, Amnesteem® into the PA policy. 2. References were reviewed and updated.	06/27/2022	07/18/2022
Policy was reviewed: 1. Initial Approval Criteria, I.A.5: Updated to remove prior concurrent therapy criteria "At least 1 of the topical agents above was used concurrently with one of the following oral antibiotics for ≥ 60 days: doxycycline, erythromycin, minocycline, tetracycline, trimethoprim-sulfamethoxazole, unless contraindicated or clinically significant adverse effects are experienced to the listed antibiotic agents." 2. Initial Approval Criteria, I.A.6: Updated to remove prior contraindication/adverse event criteria "Member has intolerance or contraindications to the excipients in generic isotretinoin." 3. Continued Therapy Approval Criteria, II.A.4: Updated to remove prior contraindication/adverse event criteria "Member has intolerance or contraindications to the excipients in generic isotretinoin." 4. References were reviewed and updated.	04/14/2023	07/13/2023
Policy was reviewed.	10/19/2023	10/19/2023