Clinical Policy Title:	isotretinoin
Policy Number:	RxA.71
Drug(s) Applied:	Claravis®, Absorica®, Absorica LD®, Myorisan®, Zenatane®, Amnesteem®
Original Policy Date:	03/06/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Isotretinoin (Claravis®, Absorica®, Absorica LD®, Myorisan®, Zenatane®, Amnesteem®) is a retinoid.

Claravis®, Absorica®, Absorica LD®, Myorisan®, Zenatane®, and Amnesteem® are indicated for severe recalcitrant nodular acne.

Absorica® and Absorica LD® are specifically indicated 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.

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

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 PO 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.

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. Failure of ≥ 2 of the following topical agents (must be from 2 different classes listed below) unless clinically significant adverse effects are experienced or all are contraindicated:
   a. Topical antibiotics: clindamycin, erythromycin;
   b. Topical anti-infectives: benzoyl peroxide 10% gel, benzoyl peroxide 10% lotion;
   c. Topical retinoids: tretinoin 0.025% gel, tretinoin 0.05% cream, tretinoin 0.1% cream;
   **Prior authorization may be required for tretinoin for age ⩾ 30 years.*
5. 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;
6. Member has intolerance or contraindications to the excipients in generic isotretinoin;
7. Dose does not exceed 2 mg/kg/day. If request is for Absorica LD®, does not exceed 1.6mg/kg/day.

Approval Duration
Commercial: 12 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If member has received 20 consecutive weeks of treatment, an 8-week treatment-free interval must be allowed prior to reinitiating isotretinoin treatment;
4. Member has intolerance or contraindications to the excipients in generic isotretinoin;
5. If request is for a dose increase, new dose does not exceed 2 mg/kg/day. If request is for dose increase of Absorica LD®, does not exceed 1.6mg/kg/day.

Approval Duration
Commercial: 12 months
Medicaid: 6 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 twice daily	Not applicable
erythromycin 2% (Erygel®, 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

Drug Name	Dosing Regimen	Maximum Dose
tretinoin (Retin-A®)	0.025% gel, 0.05% cream, 0.1% cream: Apply once daily	Not applicable
doxycycline (Monodox®)	50 to 100 mg PO daily	300 mg per day
erythromycin (EES®, Erythromycin Base®, Ery- Tab®)	250 to 500 mg PO twice daily, followed by twice daily dosing	4 gm per day
minocycline (Minocin®, Solodyn®)	IR: 100 mg PO twice daily ER: 1 mg/kg PO daily	200 mg per day
tetracycline	125 to 250 mg PO every 6 hours for 2 weeks, then 125 to 500 mg PO daily or every other day	4 mg per day
trimethoprim-sulfamethoxazole (Bactrim®)	As directed by physician	20 mg/kg/day of trimethoprim

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. Brand name might be non-preferred if generic is available.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Pregnancy (category X), hypersensitivity to the medication or any of its components.

- Boxed Warning(s):
  - If pregnancy occurs during isotretinoin use, there is an extremely high risk for severe birth defects (iPLEDGE REMS program enrollment 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

1. Isotretinoin Clinical Monograph. Clinical Pharmacology. Accessed August 13, 2019. Available at: http://www.clinicalpharmacology-ip.com. Accessed February 19, 2021.
2. Claravis™ Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; May 2018. Available at: https://dailymed.nlm.nih.gov/. Accessed February 19, 2021.
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.
4. Absorica®, Absorica® LD™: Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; Oct 2019.. Available at: http://Absorica®.com. Accessed February 19, 2021.
5. Myorisan™, Prescribing information. Lake Forest,IL. Akorn Pharmaceuticals; Updated Dec 2018. Available at https://www.akorn.com/prod_detail.php?ndc=61748-302-13. Accessed on February 19, 2021.
6. Zenatane®, Prescribing information. Princeton, NJ. Dr.Reddy's Laboratories Ltd; Updated Jan 2019. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=27b3cf26-f22e-5b70-1c24-009933b7c6ee. Accessed on February 19, 2021.
7. Amnesteem®, prescribing information. Canonsburg, PA. Mylan Pharmaceuticals Inc. Updated Aug, 2019. Available at https://www.mylan.com/en/products/product-catalog/product-profile-page?id=85abf48e-84d4-4916-a855-089435b3a992. Accessed on February 19, 2021.

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 therapeutic alternatives…". Table was also updated to remove discontinued brands Clindamax® and Desquam-X®. 4. References were updated.	02/19/2021	03/09/2021