Clinical Policy: Isotretinoin (Absorica, Absorica LD, Amnesteem, Claravis, Myorisan, Zenatane)

Reference Number: CP.PMN.143
Effective Date: 12.01.14
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

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

FDA Approved Indication(s)

Absorica, Absorica LD, Amnesteem, Claravis, Myorisan, and Zenatane are indicated for severe recalcitrant nodular acne. Absorica and Absorica LD are specifically indicated in patients 12 years of age and older.

Limitation(s) of use:
If a second course of Absorica/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.

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 Absorica, Absorica LD, Amnesteem, Claravis, Myorisan, and Zenatane are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of nodular acne;
2. Age ≥ 12 years;
3. 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*
4. At least one 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 clinically significant adverse effects are experienced or all are contraindicated;
5. If request is for Absorica or Absorica LD, member must use Myorisan, Amnesteem, Claravis, Zenatane, and generic isotretinoin unless clinically significant adverse effects are experienced or all are contraindicated;
6. Dose does not exceed one of the following (a or b):
   a. Absorica, Amnesteem, Claravis, Myorisan, Zenatane: 2 mg/kg per day;
   b. Absorica LD: 1.6 mg/kg per day.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acne (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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. If request is for Absorica or Absorica LD, member must use Myorisan, Amnesteem, Claravis, Zenatane, and generic isotretinoin unless clinically significant adverse effects are experienced or all are contraindicated;

5. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Absorica, Amnesteem, Claravis, Myorisan, Zenatane: 2 mg/kg per day;
   b. Absorica LD: 1.6 mg/kg per day.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, 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
clindamycin 1% (Cleocin T®, Clindagel®, Clindamax®)	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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
benzoyl peroxide (Desquam-X®) 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
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.

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 mild-to-moderate acne vulgaris as a Class IIa 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 Iia 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.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Isotretinoin (Absorica, Amnesteem, Claravis, Myorisan, Zenatane)	Acne	0.5 to 1 mg/kg/day PO given in two divided doses	2 mg/kg/day
Isotretinoin (Absorica LD)	Acne	0.4 to 0.8 mg/kg/day PO given in two divided doses	1.6 mg/kg/day

VI. Product Availability

Drug Name	Availability
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, and 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

VII. References

1. Absorica and Absorica LD Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; November 2019. Available at: http://absorica.com. Accessed August 23, 2022.
2. Amnesteem Prescribing Information. Morgantown, WV: Mylan Pharmaceuticals Inc; January 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b2cb63c9-f825-4991-9a2c-6260f1bbcc2c. Accessed August 23, 2022.
3. Claravis Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; January 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=a31fd109-d0fd-4ab9-ba98-a3d64333c18d. Accessed August 23, 2022.
4. Myorisan Prescribing Information. Lake Forest, IL: VersaPharm Inc.; August 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=51ff6346-9256-4c01-9f52-417d13f2df05. Accessed August 23, 2022.
5. Zenatane Prescribing Information. Princeton, NJ: Dr. Reddy's Laboratories Inc.; February 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=27b3cf26-f22e-5b70-1c24-009933b7c6ee. Accessed August 23, 2022.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed August 10, 2021.
7. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016 Feb 15;74(5):945-973.e33. doi: 10.1016/j.jaad.2015.12.037.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Modified approval duration for Medicaid and HIM to 6 months to allow adequate time to achieve the cumulative dose of 120 mg/kg-150 mg/kg as this cumulative dose is associated with lower rate of relapse and need for retreatment.	09.10.18	11.18
4Q 2019 annual review: no significant changes; added Amnesteem to policy; references reviewed and updated.	10.23.19	11.19
RT4: added Absorica LD with required step through of other isotretinoin products (including an additional product: generic isotretinoin) per SDC; removed disclaimer for NF products for HIM per pharmacy director.	03.17.20	
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.09.20	11.20
4Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	08.09.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less.	04.27.22	08.22
4Q 2022 annual review: no significant changes; converted prior trial language to "member must use" language; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.23.22	11.22

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.