Original Effective Date: 04/01/2012
Current Effective Date: 06/20/2025
Last P&T Approval/Version: 04/30/2025
Next Review Due By: 04/2026
Policy Number: C4231-C

Isotretinoin

PRODUCTS AFFECTED

Absorica (isotretinoin), Absorica LD (isotretinoin micronized), Accutane (isotretinoin), Amnesteem (isotretinoin), Claravis (isotretinoin), isotretinoin, Myorisan (isotretinoin), Zenatane (isotretinoin)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Severe Recalcitrant Nodular Acne

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. SEVERE NODULAR ACNE:
1. Documented diagnosis of severe recalcitrant nodular acne
   AND

2. Documentation of an inadequate treatment response to a 6-month trial of TWO of the following therapy regimens, with at least 3 consistent months of combination therapy with an oral and a topical agent:
   i. Topical retinoid or retinoid-like agent
   ii. Oral antibiotic
   iii. Topical antibiotic with or without benzoyl peroxide
   AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to isotretinoin include: pregnancy, hypersensitivity to the product or any of its components, avoid concomitant use with tetracyclines]

CONTINUATION OF THERAPY:

A. SEVERE NODULAR ACNE:

1. Documentation that after ≥ 2 months off therapy, persistent or recurring severe recalcitrant nodular acne is still present
   OR
2. Documentation total cumulative dose for CURRENT course of therapy is less than 150 mg/kg (will be approved up to a total up 150mg/kg) *** Isotretinoin at a dose of ≤ 0.5 mg/kg/day may be used to minimize initial flaring. A second course of isotretinoin therapy may be initiated after a period of at least two months off therapy.

DURATION OF APPROVAL:

Initial authorization: 20 weeks (20 weeks of active treatment followed by 2 months off therapy),
Continuation of therapy: 20 weeks

PRESCRIBER REQUIREMENTS:

Prescribed by a dermatologist or physician experienced in the treatment of nodular acne.

AGE RESTRICTIONS:

12 years of age and older

QUANTITY:

0.5 to 1 mg/kg/day, Max of 2 mg/kg/day for adult patients whose disease is very severe with scarring or is primarily manifested on the trunk (Absorica LD: 0.4 to 0.8 mg/kg/day and max 1.6 mg/kg/day)
Max of 150mg/kg total per course

Maximum Quantity Limits – Fewest capsules necessary to make daily dose

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Acne Products

FDA-APPROVED USES:

Indicated for the treatment of 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.

Because of significant adverse reactions associated with its use, isotretinoin is reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics.
Limitations of use: *If a second course of isotretinoin 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.*

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. Nodules are inflammatory lesions with a diameter of 5 mm or greater. The nodules may become suppurative or hemorrhagic. "Severe," by definition, means "many" as opposed to "few or several" nodules.

Because of significant adverse effects associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. In addition, isotretinoin is indicated only for those female patients who are not pregnant, because isotretinoin can cause severe birth defects (Category X). A single course of therapy for 15 to20 weeks has been shown to result in complete and prolonged remission of disease in many patients. If a second course of therapy is needed, it should not be initiated until at least 8 weeks after completion of the first course, because experience has shown that patients may continue to improve while off isotretinoin. The optimal interval before retreatment has not been defined for patients who have not completed skeletal growth.

<u>iPLEDGE Program</u>
Isotretinoin is available only through a restricted program under a REMS called the iPLEDGE REMS because of the risk of embryo-fetal toxicity. Notable requirements of the iPLEDGE REMS include the following:

- Prescribers must be certified with the program and comply with the following requirements:
  - Determine reproductive status of all patients prior to initiating treatment
  - Provide contraception counseling to patients who can get pregnant prior to and during treatment, or refer patients who can get pregnant to an expert for such counseling
  - Provide scheduled pregnancy testing, and verify and document the negative pregnancy test result prior to writing each prescription, for no more than a 30-day supply
- Patients who can become pregnant must be enrolled by signing an informed consent form and must comply with the following requirements
  - Comply with the pregnancy testing and contraception requirements
  - Demonstrate comprehension of the safe-use conditions of the program every month
  - Obtain the prescription within 7 days of the pregnancy test collection
- Patients who cannot become pregnant must be enrolled by signing an informed consent form and must obtain the prescription within 30 days of the office visit
- Pharmacies that dispense isotretinoin must be certified by being registered and activated in the program, must only dispense to patients who are authorized to receive isotretinoin, and comply with the following requirements:
  - Only dispense a maximum of a 30-day supply with a Medication Guide.
  - Do not dispense refills. Dispense only with a new prescription and a new authorization from the program.
  - Return isotretinoin to inventory if patients do not obtain the prescription by the "Do Not

Dispense To After" date

- Wholesalers and distributors must be registered with the program and must only distribute to certified pharmacies.

Further information, including a list of qualified pharmacies and distributors, is available at www.ipledgeprogram.com or 1-866-495-0654.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Isotretinoin are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Isotretinoin is absolutely contraindicated in pregnancy. Contraindications to isotretinoin include pregnancy, hypersensitivity to the product or any of its components (including parabens), avoid concomitant use with tetracyclines.

OTHER SPECIAL CONSIDERATIONS:
Isotretinoin has a Black box warning for embryo-fetal toxicity and is contraindicated in pregnancy.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Absorica CAPS 10MG
Absorica CAPS 20MG
Absorica CAPS 25MG
Absorica CAPS 30MG
Absorica CAPS 35MG
Absorica CAPS 40MG
Absorica LD CAPS 16MG
Absorica LD CAPS 24MG
Absorica LD CAPS 32MG
Absorica LD CAPS 8MG
Accutane CAPS 10MG
Accutane CAPS 20MG
Accutane CAPS 30MG
Accutane CAPS 40MG
Amnesteem CAPS 10MG
Amnesteem CAPS 20MG
Amnesteem CAPS 40MG
Claravis CAPS 10MG
Claravis CAPS 20MG
Claravis CAPS 30MG
Claravis CAPS 40MG
ISOtretinoin CAPS 10MG
ISOtretinoin CAPS 20MG
ISOtretinoin CAPS 25MG
ISOtretinoin CAPS 30MG
ISOtretinoin CAPS 35MG
ISOtretinoin CAPS 40MG
Myorisan CAPS 10MG
Myorisan CAPS 20MG
Myorisan CAPS 30MG
Myorisan CAPS 40MG
Zenatane CAPS 10MG
Zenatane CAPS 20MG
Zenatane CAPS 30MG
Zenatane CAPS 40MG

REFERENCES

1. Absorica/Absorica LD (isotretinoin) [prescribing information]. Cranbury, NJ: Sun Pharmaceutical Industries Inc; June 2023.
2. Accutane (isotretinoin) [prescribing information]. Scottsdale, AZ: JG Pharma, Inc; December 2023.
3. Amnesteem (isotretinoin) [prescribing information]. Morgantown, WV: Mylan Pharmaceuticals Inc; August 2022.
4. Claravis (isotretinoin) [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA Inc; August 2022.
5. Myorisan (isotretinoin) [prescribing information]. Lake Forest, IL: Akorn; December 2022.
6. Zenatane (isotretinoin) [prescribing information]. Princeton, NJ: Dr. Reddy's Laboratories Inc; May 2024.
7. Zaenglein, A. L., Pathy, A. L., Schlosser, B. J., Alikhan, A., Baldwin, H. E., Berson, D. S., . . . Bhushan, R. (2016). Guidelines of care for the management of Acne Vulgaris. Journal of the American Academy of Dermatology, 74(5). doi:10.1016/j.jaad.2015.12.037
8. Reynolds, R. V., Yeung, H., Cheng, C. E., Cook-Bolden, F., Desai, S. R., Druby, K., … Barbieri, J. S. (2024). Guidelines of care for the management of acne vulgaris. Journal of the American Academy of Dermatology. https://doi.org/10.1016/j.jaad.2023.12.017

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Quantity References	Q2 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity References	Q2 2024
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Prescriber Requirements FDA-Approved Uses Background Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q2 2023
REVISION- Notable revisions: Required Medical Information Prescriber Requirements References	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file