

# MTF Formulary Management for Oral Isotretinoids for Severe Recalcitrant Nodular Acne

## Defense Health Agency Pharmacy Operations Division

### Bottom Line

- Absorica is now designated with nonformulary status; all the other oral isotretinoids are Uniform Formulary.
- No oral isotretinoids were placed on the Basic Core Formulary.
- Manual prior authorization applies to all new users of Absorica; current Absorica users are grandfathered.
- All isotretinoin products have the same indication, efficacy, and safety profiles.
- Myorisan and Amnesteem are the most cost-effective oral isotretinoin products. Zenatane is noncompliant with the Trade Agreements Act (TAA); therefore, MTFs may NOT purchase it.

**Uniform Formulary Decision:** The Director, DHA, approved recommendations from the November 2015 DoD P&T Committee meeting on January 29, 2016, with an implementation date of May 4, 2016.

Uniform Formulary (UF) Oral Isotretinoids		Nonformulary Oral Isotretinoids
Oral Isotretinoids on BCF MTFs <u>must</u> have on formulary	Oral Isotretinoids not on BCF MTFs <u>may</u> have on formulary	MTFs <u>must not</u> have on formulary
None	Generic formulations of Accutane: Amnesteem, Claravis, and Myorisan, Zenatane* *Noncompliant with TAA	Absorica

### Clinical Summary

- The oral isotretinoids all contain the same active ingredient and are indicated for the treatment of severe nodular recalcitrant acne in patients 12 years of age and older.
- The original branded product in the class, Accutane, was discontinued from the market. The generic formulations of Accutane include Amnesteem, Claravis, Myorisan, and Zenatane.
- In the MTF setting, Amnesteem is the most prescribed and most cost-effective oral isotretinoin.
- The oral isotretinoids require a total cumulative dose of 120–150 mg/kg, taken over 15–20 weeks, to clear severe acne and reduce the risk of relapse. These products should be taken with fatty meals (preferably containing at least 50 grams of fat) to ensure adequate absorption.
- Absorica is an oral isotretinoin product approved under a New Drug Application (NDA) that is specifically formulated to allow for absorption regardless of meals. In a fasting state, the area under the curve (AUC) for Absorica is higher (67%) versus generic formulations of oral isotretinoin (40%).
- In one head-to-head comparison of Absorica with generic isotretinoin, there was no difference in efficacy between the two products when administered with fatty meals. Similarly, there were no significant differences in safety profiles between the two products.
- There are no head-to-head trials that indicate improved compliance or less risk of relapse of nodular acne with Absorica compared to the generic oral isotretinoids.
- Prescribers of oral isotretinoin therapy are encouraged to try Amnesteem, Claravis, and Myorisan before using Absorica, which requires manual Prior Authorization. Limit Absorica to patients who are unable to comply with dietary requirements associated with use of the other oral isotretinoin products.

### Safety & Tolerability

- Due to the potential for teratogenicity, the use, prescribing, and dispensing of oral isotretinoin requires enrollment of patients, prescribers, and dispensing pharmacies in the FDA's iPLEDGE Program.
- All the oral isotretinoids are rated as pregnancy category X, due to the extremely high risk of severe birth defects. Isotretinoin must not be used in female patients who are or who may become pregnant.
- Serious adverse events associated with the oral isotretinoids include (1) psychiatric disorders, such as depression, anxiety, psychosis, suicidal ideation; and, (2) pseudotumor cerebri (avoid concomitant tetracycline use).

- The most common side effects among all isotretinoin (occurring at an incidence >5%) include the following: dry lips, dry skin, dry eyes, dermatitis, nasopharyngitis, epistaxis, cheilitis, arthralgia, reduction in visual acuity, back pain, musculoskeletal discomfort, and increased blood creatine kinase levels.

**Oral Isotretinoin Comparison Table**

Parameter	Absorica	Amnesteem	Claravis	Zenatane	Myorisan
<b>Frequency of Administration</b>	All isotretinoin must be taken twice daily				
<b>Dietary Requirement</b>	Regardless of meals	Must be taken with meals			
<b>Strengths</b>	10mg, 20mg, 25mg, 30mg, 35mg, 40 mg	10mg, 20mg, 40 mg		10mg, 20mg, 30mg, 40 mg	
<b>Packaging and Delivery Systems</b>	3 x 10s: 3 Blister Packs in 1 Carton (10 capsules/ Blister Pack)			<ul style="list-style-type: none"> <li>3 Blister Packs/ Carton (10 caps/ pack)</li> <li>10 Blister Packs/ Carton (10 caps/ pack)</li> <li>5,000 capsules</li> </ul>	
<b>REMS Requirement</b>	Mandatory iPLEDGE registration, max 30-day supply dispensed at one time with no refills				
<b>Bioequivalence and Interchangeability</b>	BX-rated; not interchangeable with other drugs listed in this table	AB-rated bioequivalence to innovator Accutane. All the generic products are therapeutically interchangeable with each other (except with Absorica).			

**References**

- DoD P&T Committee minutes: <http://www.health.mil/PandT>
- Current/future drug classes under review by the DoD P&T Committee: <http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee>
- TRICARE Formulary Search Tool: <http://www.health.mil/formulary>
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents (including this one) available at: <http://www.health.mil/DoDPTResources>
- Point of contact for additional information: [dha.jbsa.pharmacy.list.poduf@mail.mil](mailto:dha.jbsa.pharmacy.list.poduf@mail.mil)

Oral Isotretinoin Price Comparison at MTF	
Drug	MTF Cost/Month (November 2015)
<b>Basic Core Formulary</b>	
None	
<b>Uniform Formulary</b>	
Myorisan	<b>\$ Most Cost-Effective</b>
Amnesteem	<b>\$ Most Cost-Effective</b>
Claravis	<b>\$\$ Less Cost-Effective</b>
<b>Nonformulary</b>	
Absorica	<b>\$\$\$\$ Least Cost-Effective</b>
Legend:	
<b>\$</b> = "Most Cost-Effective" represents Rx's with the lowest cost and/or best clinical efficacy	
<b>\$\$</b> = "Less Cost-Effective" represents higher cost Rx's with similar clinical efficacy	
<b>\$\$\$\$</b> = "Least Cost-Effective" represents Rx's with the highest cost with similar clinical efficacy	