

hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements: Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is 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.

FDA-APPROVED INDICATION

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 females who are not pregnant, because isotretinoin can cause severe birth defects.

A single course of therapy for 15 to 20 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.

Special Prescribing Requirements: Because of isotretinoin's teratogenicity and to minimize fetal exposure isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration (FDA). This program is called iPLEDGE™. The iPLEDGE program is a computer-based risk management system that uses verifiable, trackable links between prescriber, patient, pharmacy, and wholesaler to control prescribing, using, dispensing and distribution of isotretinoin.

Medical Necessity Guideline:

The following questionnaire may be used to determine medical necessity of Accutane, Amnesteem, Claravis and Sotret prescriptions.

CRITERIA FOR APPROVAL

- | | | |
|--|-----|----|
| 1. Does the patient have a diagnosis of acne (e.g., severe [recalcitrant] nodulocystic acne, mild to moderate acne vulgaris, or cystic acne?)
[If the answer to this question is yes, may skip to question 4.] | Yes | No |
| 2. Does the patient have a one of the following off-label diagnoses?
-carcinoma (e.g., basal cell carcinoma, squamous cell carcinoma)
-malignant neoplasm (e.g., cutaneous T-cell lymphoma, neuroblastoma)
-psoriasis
-severe refractory rosacea
[If the answer to this question is yes, skip to question 6.] | Yes | No |
| 3. Does the patient have a diagnosis of severe Keratinization Disorders?
(e.g., keratosis follicularis (Darier-White disease), pityriasis rubra pilaris, lamellar ichthyosis, ketatosis palmaris et plantaris, congenital ichthyosiform erythroderma, lichen planus)
[If the answer to this question is yes, may skip to question 6.]
[If the answer to this question is no, then no further questions required.] | Yes | No |
| 4. Has the patient tried and had insufficient response to at least a 3 month trial of systemic antibiotics? | Yes | No |

5.	Has the patient tried and failed at least a one month trial of any of the following treatments in addition to systemic antibiotics? - Topical antibiotics (for example: topical clindamycin or topical erythromycin) - Benzoyl peroxide products (Oxy-10, Benzac) - Topical retinoids (for example: Retin-A, Avita,)	Yes	No
6.	Does the patient exhibit any signs and symptoms of significant depression, psychosis or suicide potential?	Yes	No
7.	Is patient currently taking a tetracycline class product? [If no, skip to question 9.]	Yes	No
8.	Will the tetracycline class product be discontinued prior to isotretinoin therapy?	Yes	No
9.	Has the patient taken a previous course (up to 20 weeks) of oral isotretinoin therapy? [If answer is no, no further questions needed.]	Yes	No
10.	Has the patient been off therapy for at least 8 weeks?	Yes	No
11.	Has the patient received 2 courses (up to a total of 40 weeks) of oral isotretinoin therapy?	Yes	No

Guidelines for Approval							
Duration of Approval				5 months			
Set 1		Set 2		Set 3		Set 4	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	6	1	6	1	6	1	6
4	7	4	7	4	9	4	11
5	9	5	11	5		5	
		9		7		7	
		10		8		8	
						9	
						10	
Set 5		Set 6		Set 7		Set 8	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
2	1	2	1	2	1	2	1
	6	9	6	7	6	7	6
	7	10	7	8	9	8	11
	9		11			9	
						10	
Set 9		Set 10		Set 11		Set 12	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
3	1	3	1	3	1	3	1
	2	9	2	7	2	7	2
	6	10	6	8	6	8	6
	7		7		9	9	11
	9		11			10	

Horizon BCBSNJ Pharmacy Guideline Development Process: This Horizon BCBSNJ Pharmacy Guideline (the "Pharmacy Guideline") has been developed by Horizon BCBSNJ's Pharmacy Drug Policy Subcommittee, Clinical Issues Subcommittee, and Quality Improvement Committee which include practicing physicians and pharmacists. This guideline is consistent with generally accepted standards of medical and pharmacy practice, and reflects Horizon BCBSNJ's view of the subject health care services, supplies drugs or procedures, and in what circumstances they are deemed to be medically necessary or experimental/ investigational in nature. This Pharmacy Guideline also considers whether and to what degree the subject health care services, supplies or procedures are clinically appropriate, in terms of type, frequency, extent, site and duration and if they are considered effective for the illnesses, injuries or diseases discussed. Where relevant, this Pharmacy Guideline considers whether the subject prescription drugs are being requested primarily for the convenience of the covered person or the health care provider. It may also consider whether the prescription drugs are more costly than alternative prescription drugs that are at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the relevant illness, injury or disease. In reaching its conclusion regarding what it considers to be the generally accepted standards of medical and pharmacy practice, Horizon BCBSNJ reviews and considers the following: all credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, physician and health care provider specialty society recommendations, the views of physicians and health care providers practicing in relevant clinical areas (including, but not limited to, the prevailing opinion within the appropriate specialty), the findings and directives of the Food and Drug Administration and any other relevant factor as determined by applicable State and Federal laws and regulations.

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and for compendia uses. 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 side effects and risks associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics and who have been notified of the risks associated with isotretinoin treatment. Isotretinoin must not be used by female patients who are or may become pregnant.

Isotretinoin will also be covered for the compendia uses of acne vulgaris or cystic acne, carcinoma (basal cell carcinoma, squamous carcinoma), malignant neoplasm (cutaneous t-cell lymphoma, neuroblastoma), psoriasis, severe refractory rosacea, severe keratinization disorders (keratosis follicularis (Darier-White disease), pityriasis rubra pilaris, lamellar ichthyosis, keratosis palmaris et plantaris, congenital ichthyosiform erythroderma, lichen planus)..

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.

To receive one additional course of therapy, the patient should have at least an 8-week untreated period before retreatment, must have had success with initial therapy but is now experiencing recurring severe nodular acne (and a negative pregnancy test if female). It is important that isotretinoin be given at the recommended doses and for no longer than the recommended duration. There is no safety information for use beyond 20 to 40 weeks.

REFERENCES

1. Accutane Product Information. Roche Pharmaceuticals. August 2005.
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9. National Institute of Health Office of Rare Diseases. Available at:

<http://rearediseases.info.nih.gov/asp/diseases/diseses.asp>.

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