FOR PHYSICIAN REVIEW: CIPHER PHARMACEUTICALS

On behalf of Cipher Pharmaceuticals, we would like to thank you for your dedication in looking after new and existing dermatology patients during this difficult COVID 19 pandemic. By practicing virtual diagnosis and treatment, you continue to provide excellent patient care to our healthcare community.

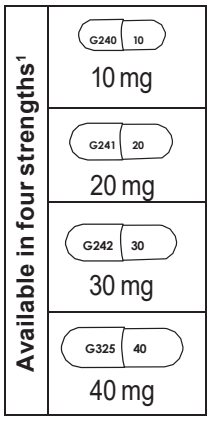
We would also like to ensure you that EPURIS® is in full supply across the country and we remain committed to continuing to support the Canadian dermatology community as we move forward during and post this pandemic. If you require any further medical or patient information regarding EPURIS®, please don't hesitate to reach out to us at the contact information listed below.

Pr epuris® isotretinoin capsules

Epuris® is indicated for patients who have severe nodular and/ or inflammatory acne, acne conglobata and recalcitrant acne.[1]

Because of significant side effects associated with its use, Epuris® should be reserved for patients where the conditions listed above are unresponsive to conventional first line therapies.[1]

Epuris® capsules should not be substituted with other isotretinoin-containing products.[1]



Prescribe Epuris® for your patients with severe acne:

- Absorbed in the fasted and non-fasted state[1,2]
- Flexible dosing with four strengths[1]
- Safety profile was consistent with the clinically proven safety profile of isotretinoin†[1]

For more information contact Cipher at 1-855-437-8747 (1-855-4-EPURIS). Ask us about educational materials and a support program to help educate your patients on Epuris® treatment.

† Double-blind, randomized, Phase 3, parallel group study of Epuris® vs. isotretinoin (reference product) under fed conditions in 925 patients with severe recalcitrant nodular acne.

Clinical use:

Epuris® should only be prescribed by physicians knowledgeable in the use of retinoids systemically, who understand the risk of teratogenicity in females of child bearing age and who are experienced in counselling young adults for whom isotretinoin is generally indicated. **Epuris® should not be substituted with other marketed formulations of isotretinoin.** A careful assessment of the patient's mental state should be made, including whether or not they have a history of previous psychiatric illness.

It is strongly recommended that each Epuris® prescription be limited to a one-month supply in order to encourage patients to return for follow-up to monitor side-effects.
Continuation of treatment requires a new prescription. Ideally, pregnancy testing, issuing a prescription and dispensing of EPURIS should occur on the same day.

Dispensing of EPURIS should occur within a maximum of 7 days of the prescription.

The use of Epuris® in pediatric patients less than 12 years of age is not recommended. The use of isotretinoin for the treatment of severe recalcitrant nodular acne in pediatric patients ages 12 to 17 years should be given careful consideration, especially for those patients where a known metabolic or structural bone disease exists.

Contraindications:

Pregnancy while taking Epuris® or for at least one month after its discontinuation; breastfeeding women; hepatic and renal insufficiency; hypervitaminosis A; patients with excessively elevated blood lipids; patients taking tetracyclines; patients who are sensitive to isotretinoin or to any of the excipients.

Epuris® should only be prescribed by physicians knowledgeable in the use of retinoids systemically.

Most serious warnings and precautions:

The Information/Consent/Agreement should be signed by all patients prior to starting therapy with isotretinoin

Pregnancy prevention: Isotretinoin is a known teratogen contraindicated in pregnancy. Physicians should **only** prescribe Epuris® to females of childbearing potential if **ALL** the conditions described in the Product Monograph under "Conditions of use" are met: patient has severe disfiguring nodular and/ or inflammatory acne, acne conglobate or recalcitrant acne that has not responded to standard therapy; patient can understand and carry out instructions; patient must sign the informed consent form prior to therapy; patient is willing to comply with mandatory effective contraceptive measures; patient understands the hazards of fetal exposure to isotretinoin and the risk of possible contraception failure; patient understands the need to rapidly consult her physician if there is a risk of pregnancy; patient understands the need for monthly follow-up; patient uses effective contraception; patient has had two negative pregnancy tests and two or three days of the next normal menstrual period before starting Epuris® therapy; in the event of relapse treatment, the patient must also use the same uninterrupted and effective contraceptive measures one month prior to, during and for one month after Epuris®. In addition, when prescribing this drug to female patients of childbearing potential, physicians **MUST** use the **Epuris® Patient Engagement and Education Resource (PEER™) Program**. The program information can be accessed at www.epuris.ca.

Psychiatric: Some patients treated with isotretinoin have become depressed and some attempted or committed suicide. Although a causal relationship has not been established, all patients should be screened and monitored for signs of depression during therapy.

Neurologic: Isotretinoin use has been associated with a number of cases of pseudotumor cerebri (benign intracranial hypertension), some of which involved concomitant use of tetracyclines. Early symptoms of pseudotumor cerebri include headache, nausea and voting, and visual disturbances. Patients with these symptoms should be screened for papilledema and, if present, the drug should be discontinued immediately and the patient referred to a neurologist for diagnosis and care. Concomitant treatment with tetracyclines should be avoided.

Other relevant warnings and precautions:

Serious skin reactions; blood donation; cardiovascular; impaired hearing at certain frequencies; diabetes or a family history of diabetes; gastrointestinal: inflammatory bowel disease; anaphylactic reactions; musculoskeletal; hyperostosis; ophthalmologic; acute exacerbation of acne;

Monitoring and laboratory tests:

Pregnancy tests; signs of depression, serum blood lipid determinations; completed blood count and differential, liver function tests, blood glucose levels;

Geriatrics (>65 years of age):

Unknown whether they respond differently from younger subjects but effects of aging might be expected to increase some risks associated with isotretinoin therapy.

For more information:

Please consult the Product Monograph at www.epuris.ca for important information relating to adverse reactions, drug interactions, and dosing information. The product monograph is also available by calling us at 1-855-437-8747 (1-855-4-EPURIS).

References: 1. Cipher Pharmaceuticals Inc. Epuris® Product Monograph. July 26, 2019.; 2. Under fasted conditions, it was observed that the mean AUC_{0-t} and C_{max} were approximately 33% and 20% lower than that observed under high fat-fed conditions.

cipher™ PHARMACEUTICALS

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