

Dear SAB Member:

On September 14, 2012 the iPLEDGE Program Non-Compliance Action Policy (NCAP) went into effect for the iPLEDGE Program in order to codify the Program's ongoing non-compliance efforts. As a part of the Sponsors' efforts to further improve the effectiveness of the NCAP based on lessons learned since the NCAP was implemented, ***beginning on December 31, 2015 the Sponsors will implement a revision to the NCAP*** (see attached), which we'd appreciate your help in disseminating to the members of your respective organizations.

Version 6 of the NCAP includes changes to Section 7 (Investigation and Action Implementation). The following statement will be added to Section 7.2 "Non-Compliance by designees – Impact to prescriber status":

- The registered prescriber is responsible for all information entered, and activities performed, in the iPLEDGE Program by the office staff designee(s).

Changes to Section 9, Table 2 (additions and modifications to typical stakeholder Non-Compliance activities) will include the following:

Prescriber

- Warning
 - Section 9.A.2.xii. Prescriber's designee performed activities in the iPLEDGE Program system that indicate lack of training and/or supervision

Designee

- Warning
 - Section 9.B.2.xii. Designee registered as a prescriber

Pharmacy

- Warning
 - Warning Accumulation and Suspension
 - 1 Warning while in a Suspended status will result in Permanent Deactivation
 - 1 Warning while in a Temporary Deactivation status will result in Permanent Deactivation
- Permanent Deactivation
 - Section 9.C.4.vi. 1 Warning while in a Temporary Deactivation status

Wholesaler

- Warning
 - Section 9.D.2.vi. Wholesaler package adulteration (re-packaging of product from original state)

Section 11 was added to introduce the monitoring and investigative process for stakeholders suspected of intentional falsification of patient classification type.

- **Monitoring and Investigation for Patient Misclassification (Refer to sections 9.A.4.v. and 9.B.4.iv.): Intentional falsification of patient classification type determined to be an attempt to violate program requirements**

- **Patients in the iPLEDGE Program must be classified correctly into one of three categories: Female of Reproductive Potential (FRP), Female of Non-Reproductive Potential (FNRP), or male. Prescribers and designees who have a significantly higher percentage of a particular patient category (compared to the program average) or other anomalies may be investigated.**

The iPLEDGE Program actively monitors patient classification data. Prescribers/designees may be investigated based upon these data.

Please share the above changes, as well as the attached document, with the members of your respective organizations as soon as possible to ensure smooth implementation of this revised iPLEDGE Program NCAP, which *will become effective on December 31, 2015.*

Please feel free to reply to this email with any questions you may have. Thank you in advance for your assistance in disseminating this important information regarding the iPLEDGE Program.

Sincerely,

The iPLEDGE Program Sponsors

Attachments:

- (1) Non-Compliance Action Policy

Safety Notice

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE™. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lipids, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.

Links to Package Inserts

Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions at:

- Absorica: <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=8d54aab5-3349-4a41-8533-0a566fd7bbaa>
- Amnesteem: <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=b2cb63c9-f825-4991-9a2c-6260f1bbcc2c>
- Claravis: <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=a31fd109-d0fd-4ab9-ba98-a3d64333c18d>
- Myorisan: <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=51ff6346-9256-4c01-9f52-417d13f2df05>
- Sotret: <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=d5a26c5e-9c3e-4781-8c08-62b91d21a68d>
- Zenatane: <http://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=zenatane>