November 29, 2021

Patrizia Cavazzoni, MD
Director, Center for Drug Evaluation and Research
Food and Drug Administration
25 New Hampshire Avenue
Silver Spring, Maryland 20903

Submitted electronically to Patrizia.Cavazzoni@fda.hhs.gov

Dear Director Cavazzoni,

On behalf of the nearly 16,500 U.S.-based members of the American Academy of Dermatology Association (AADA), we write to urge the United States Food and Drug Administration to temporarily halt the iPLEDGE Risk Evaluation and Mitigation Strategy (REMS) program beginning December 13, 2021, to allow patients to obtain isotretinoin directly from their pharmacies.

Syneos Health recently notified dermatologists that the iPLEDGE Sponsors plan to transition this REMS program to a new platform and to mandate new requirements for prescribers that may restrict patient access to isotretinoin. Many patients on the medication will be unable to access it for at least a month due to the system changes proposed, which will cause considerable patient harm. Patients in the "able to become pregnant" category may suffer additional delays due to the requirement to record a negative pregnancy test *at the enrollment visit, which adds additional barriers to access*. We are very concerned that the proposed requirements will discourage practitioners from enrolling new patients who need isotretinoin into iPLEDGE due to the barriers imposed by these system changes.

The new requirements of concern include:

1. Requiring patient data be manually entered into the new platform over a 3-day period, which may prevent patients from claiming their medication.
2. Requiring prescribers to obtain supervised electronic written consent from patients during an office visit. This may not be possible for practices with no access to a web browser in patient exam rooms. In addition, this requirement, even if achievable, is likely to extend visit time length, thereby disrupting or delaying the rooming of other patients, which as a downstream effect could contribute to longer wait times for appointments of *all* patients, not just those on isotretinoin.

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3. Requiring patients to appear *in the physician office* with proof of a negative pregnancy test at the time of enrollment will result in the need for additional visits to start isotretinoin if an in-office pregnancy testing is not available and will prevent much needed use of telemedicine during the public health emergency.

The iPLEDGE program sponsors and their consultant, Syneos Health, developed these requirements without consulting prescribers. The Sponsors are unwilling to postpone these changes to allow for modifying the requirements. These changes may increase existing health disparities by further reducing access for patients already less likely to have access to participating pharmacies and less likely to complete a course of therapy with isotretinoin.[1] The logistical challenges posed by the proposed changes may worsen the situation, by increasing patient visits, and exacerbating health literacy, technology, and language barriers. The additional administrative burdens may cause clinicians to stop prescribing isotretinoin altogether, (which is what was seen with the initial introduction of iPLEDGE).[2]

Isotretinoin is sound and appropriate therapy to treat severe acne vulgaris and nodulocystic, but also used off-label to treat patients with a variety of other serious skin conditions such as ichthyoses, cutaneous T-cell lymphoma, patients with multiple skin cancers used for skin cancer prevention, acneiform eruptions due to chemotherapy, and neuroblastoma among others. The abrupt halting of therapy may worsen a patient's skin disease.

We urge the FDA to temporarily halt the iPLEDGE REMS program and to work closely with the program administrators to address these challenges and avoid interruptions in patient care. We welcome the opportunity to meet with you and discuss the matter further and hopefully resolve this issue of patient access to isotretinoin. AJ Custard, JD, Manger, Regulatory Policy, will be our primary point of contact on this issue. He can be reached at (202) 230-6650 or ajcustard@aad.org.

Sincerely,

Ken Tomecki

Kenneth J. Tomecki, MD, FAAD
President, American Academy of Dermatology Association

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[1]Charrow A, Xia FD, Lu J, Waul M, Joyce C, Mostaghimi A. Differences in isotretinoin start, interruption, and early termination across race and sex in the iPLEDGE era. PLoS One. 2019 Mar 26;14(3):e0210445. doi: 10.1371/journal.pone.0210445. PMID: 30913210; PMCID: PMC6435230. https://pubmed.ncbi.nlm.nih.gov/30913210/

[2] Pinheiro SP, Kang EM, Kim CY, Governale LA, Zhou EH, Hammad TA. Concomitant use of isotretinoin and contraceptives before and after iPledge in the United States. Pharmacoepidemiol Drug Saf. 2013 Dec;22(12):1251-7. doi: 10.1002/pds.3481. Epub 2013 Aug 3. PMID: 23913625. Pinhiero study Fig 2 https://pubmed.ncbi.nlm.nih.gov/23913625/