



A Listening Session on Pemphigus and Pemphigoid

Monday, February 8, 2021

The US Food and Drug Administration (FDA) held a Listening Session with patients representing the International Pemphigus & Pemphigoid Foundation (IPPF) on February 8, 2021. Patient Listening Sessions are intended to be an opportunity for the FDA's medical product centers to engage with patients and their advocates. The IPPF session was patient-led, meaning that the IPPF requested and received the permission to share its members' perspectives with the FDA.



Session Objective

The objective for this listening session was to have a dialogue with the FDA to share the emotional experience of the patient journey as well as the burden these diseases have on all aspects of a person's life. This includes the time it takes to get a diagnosis, the burdens of treatment options, and the undertreated areas of the diseases that affect the physical, emotional/psychological, and financial health of five pemphigus and pemphigoid patients.

Summary of Topics Discussed

Pemphigus and pemphigoid are rare, ultra-orphan, autoimmune, blistering diseases that result in potentially life-threatening destruction of the skin and mucosa. The patient's immune system makes antibodies that attack healthy cells in the skin or mucous membranes. As a result, skin cells separate from each other, fluid collects between skin layers, and blisters form. These blisters may cover a large area of skin. This results in fragile, extremely tender lesions that do not go away without proper treatment. It takes the average pemphigus or pemphigoid patient five healthcare providers and ten months to obtain a correct diagnosis. Currently, no cure exists for pemphigus or pemphigoid, only treatments and remission.

According to recent literature in the *British Journal of Dermatology*, pemphigus is rarer than pemphigoid. The approximate incidence of pemphigus is .58 - .80:100,000 people, and the approximate incidence of pemphigoid is 7.3 - 7.93:100,000 people.

These diseases are known to affect people across gender, racial, and cultural lines. However, there are certain groups of people who have a higher incidence of the diseases, such as Eastern Europeans of Jewish descent and people of Mediterranean, Northern India, and Persian descent.

Diagnostic Delays

For a definite diagnosis, doctors consider the clinical presentation and visual exam of oral and skin lesions. Many times, a lesional biopsy is taken and examined under a microscope for traditional histology and exam (H&E). Additionally, the layer of skin in which cell-to-cell separation occurs can be determined. Frequently, direct immunofluorescence is used to look at a treated skin sample to detect desmoglein antibodies in the skin. Indirect immunofluorescence or antibody titer test is also used to measure the autoantibodies in the blood serum.



All patients described the journey from first seeking care to a final diagnosis of pemphigus or pemphigoid. Without exception, it took months to years to achieve diagnosis, with multiple practitioners being consulted and many instances of incorrect diagnosis. The IPPF commissioned a study in 2011 and found that the average patient had to see five different healthcare providers over the course of ten months to receive a correct diagnosis. Ten percent of respondents in that study reported having to see over ten healthcare providers to receive a correct diagnosis.

Each of the five patients who participated in the Patient Listening Session described how their disease started with benign symptoms that were explained away as oral canker sores, a sore throat, a bug bite, tonsillitis, or other common problems. Patients described a vast decrease in their quality of life and a loss of independence as the disease progressed and their health deteriorated. As members of the military, a single mother, a pilot, and a young healthcare administrator, these patients were strong and independent, but they eventually had to move in with family members, rely on others for personal around-the-clock care, and even declare bankruptcy from losing the ability to work.

Working was difficult, and many with pemphigus and pemphigoid experience bias based on having skin lesions. The IPPF Founder described how she lost her job due to her skin lesions because she no longer looked clean and healthy. Another on the panel described how he could no longer pilot an airplane according to FAA guidelines due to the dose of prednisone he had been prescribed. Another described laying in a hospital ICU wrapped up “like a mummy.” The financial burden of having pemphigus or pemphigoid is greatly related to a patient’s inability to work or to do their job in the same way. Patients are further burdened by using off-label treatments that are not part of an insurance formulary for pemphigus and pemphigoid.

Treatment Options

Pemphigus and pemphigoid are chronic illnesses that, with rare exception, do not improve without active treatment. Treatment approaches include a control phase, a consolidation phase, and a maintenance phase, with the possibility of complete remission or disease relapse (flare).

Initial therapy is determined by the extent and rate of the progression of lesions. This includes the control and consolidation phases of treatment. The priority is to control lesions. In a slow, progressive form of the disease, initial treatment usually includes oral and topical corticosteroids, as well as intralesional injections of corticosteroids.



In the consolidation phase, drugs and doses are maintained until complete clearance of lesions.

Once most lesions have healed, the dose and type of medication are gradually reduced to limit the risk of side effects. This is the maintenance phase. The rate of dose reduction is determined by clinical response and overall disease activity. It is important to monitor this balance and limit use of unnecessary medication as many fatalities are related to complications with therapy.

Relapse may occur at any time, resulting in renewed disease control efforts.

Currently, Rituximab is the only FDA approved therapy for moderate to severe pemphigus vulgaris.

Other off-label therapies include immunosuppressants, intravenous immunoglobulin, and anti-inflammatory agents.

Investigational therapies currently being researched include monoclonal antibodies, Anti-C5aR Antibody, CAAR-T cell therapy, BTK inhibitors, FcRn receptors, and other recombinant small proteins that reduce the immune/inflammatory response.

All five patients shared the treatment plans they were given upon their diagnosis of pemphigus or pemphigoid. Prednisone was consistently used as an early treatment, and it is also still being prescribed as a part of step therapy. The doses stated were high—up to 0.5 - 1 mg per kilogram of body mass. This created additional physical and mental health issues, such as weight gain, anxiety, depression, social isolation, hypertension, and mood swings.

Further treatments often involve off-label usage, leading to both delays in prescription and insurance coverage issues.

Two of the five patients who participated in the Listening Session were not in remission, but they both felt that their prior experiences, coupled with an increase in available information and support, made it easier to cope with flares.

Medical Burdens

All patients commented on the pain involved with their disorders. The pain associated with blistering was accompanied with pain from the dressing of blistering locations and, in some cases, by treatment associated with an incorrect diagnosis.



Investigational Research

The IPPF reviewed some of the major research and trials being conducted.

Mental & Social Burdens

Patients present had diagnosis dates as recent as three years and as distant as over thirty years. Those with a less recent diagnosis were often exposed to statements such as, “this disease is fatal,” in pre-internet sources.

In many instances, the disorder was noted to be disfiguring. This caused alienation and a feeling of shame in some cases. Once blistering was controlled, there was still the potential for long-term scarring.

All patients reported the opinion that these conditions could not be faced alone. All had a support system beyond the medical practitioners involved in their care. For many, work became difficult or impossible, with the associated shortfalls in income and insurance coverage. Additionally, some treatments required infusions that took 7 - 8 hours to administer and had side-effects that lessened patients’ ability to work.

FDA Divisions Present

Center for Drugs

Center for Biologics

Center for Medical Devices

Reagan-Udall Center

Office of the Director



Patients Represented

Patient	Disease State	Demographics
1	Pemphigus Vulgaris	White. Female, 70s
2	Pemphigus Foliaceus	Hispanic, Male, 40s
3	Pemphigus Vulgaris	White, Male, 40s
4	Pemphigus Vulgaris	African American, Female, 40s
5	Bullous Pemphigoid	White, Female 50s

Disclaimer

Discussions in FDA Rare Disease Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on the FDA and all other participants. This report reflects the IPPF's account of the perspectives of patients and caregivers who participated in the Rare Disease Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of pemphigus and pemphigoid, health effects and impacts, and treatment experiences reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire pemphigus and pemphigoid patient population, or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.