September 27, 2021

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Ref: Xolair (omalizumab) subcutaneous injections

Policy #2021D0033T (UHC Commercial Plan)
Effective Date: 10/01/2021

Policy #CS2021D0033V (UHC Community Plan)
Effective Date: 08/01/2021

Dear Mr. Lagerstrom and Dr. Docimo:

The Advocacy Council of the American College of Allergy, Asthma and Immunology (ACAAI) together with its sponsoring organization, the ACAAI, appreciate this opportunity to discuss United Healthcare's (UHC) policy (noted above) pertaining to the administration of Xolair. The Advocacy Council and the ACAAI represent the interests of over 6,000 allergists-immunologists, allied health professionals and the patients they serve. Its members provide patient services across a variety of settings ranging from small or solo physician offices to large academic medical centers.

Ours concerns regarding the policies noted above, pertain to the administration of Xolair. Effective October 1, 2021, these policies shift in-office administration of Xolair by a healthcare professional to self-administration at home. **As such, these policies raise significant concerns pertaining to safety, adherence, costs, patient-physician relationships, and equity of healthcare that will negatively affect overall healthcare outcomes.** These policies also impose a higher administrative burden on an already stressed healthcare system for both patients and physicians, further worsening the negative impact caused by the current COVID-19 pandemic. If UHC allows these policies to become effective, they would also negatively affect under-represented minorities who already experience disproportionately poorer outcomes in healthcare and would strip patients and physicians from the vitally important benefit of shared decision making.

Xolair was approved by the Food and Drug Administration for allergic asthma in 2003 as a result of pivotal trials confirming statistically significant reductions in asthma exacerbations compared to placebos. Since the approval of Xolair, there has been an exhaustive number of controlled, real-world and retrospective studies confirming the efficacy of Xolair. Subsequently, Xolair has been approved for the treatment of chronic spontaneous urticaria (CSU) and nasal polyposis (NP). **All these studies were performed in physician office-based settings. As such, outcomes, adherence, correct administration, and safety of the Xolair injection was precisely monitored.**

Patient Safety
In the asthma trials, treatment with Xolair significantly reduced asthma exacerbations when compared to baseline (pre-enrollment) treatment with placebo. There is no question that this improvement was due in-part to the correct administration of Xolair by a healthcare professional, supervised by a physician who is physically present with the patient while monitoring for asthma control, adjusting baseline asthma therapy when needed, and ensuring adherence. Also, appropriate drug delivery and correct storage were maintained during these trials. All these factors would be lost if patients were forced to self-administer Xolair at home and would result in overall worsened outcomes.

While the overall safety of Xolair has been proven, due to the high incidence of adverse allergic reactions such as anaphylaxis, Xolair received a "box" warning for anaphylaxis from the FDA. This box warning states:

> *"Initiate Xolair therapy in a healthcare setting and closely observe patients for an appropriate period of time. Healthcare providers should be prepared to manage anaphylaxis which can be life-threatening."*

The literature also confirms that 30% to 40% of anaphylactic episodes occur after the third dose. Therefore, the upcoming UHC policy change - of only receiving the first three doses in a healthcare facility - raise further concern for patient-safety. Because 30% to 40% of anaphylactic episodes occur after the third dose, UHC is placing the patient in significant danger of complications from anaphylaxis. Furthermore, this policy places the burden of identifying and treating anaphylactic symptoms on the patient or caregiver, adding to the increased risks of self-administration at home.

Although Xolair is not available as an "autoinjector", the "Xolair self-injection with prefilled syringe patient identification guide" from the manufacturer states that not only should Xolair be initiated in a healthcare setting due to the risk of anaphylaxis and need for monitoring, but that a healthcare provider should determine if it is in the patient's best interest to continue Xolair administration in a healthcare setting, based on careful assessment of risk factors for anaphylaxis and mitigation strategies.

Because risk factors for anaphylaxis to Xolair include prior history of anaphylaxis to many other agents, Xolair should NOT be self-administered at home if there is a history of anaphylaxis to other agents such as foods, drugs, biologics, etc. The UHC policy states that "a prior history of severe hypersensitivity reaction to Xolair within the past six months" is the only safety criteria for allowing continued administration in a healthcare facility. In fact, Xolair is usually discontinued when a severe hypersensitivity reaction occurs. As noted, Xolair is not available as an autoinjector, and clearly prefilled syringes are difficult and challenging to self-administer. The manufacturer's guide also recommends that pediatric patients should have a healthcare professional administer injections. Finally, the guide states that self-administration at home may be hindered by:

> *"Physical or mental impairments, inability to communicate with specialty pharmacy relative to shipment and storage of Xolair, unwillingness to self-administer, and inability to manage potential adverse events."*

The published post-marketing incidence of anaphylaxis is 0.2% and other publications have confirmed that Xolair was the number one cause of drug-induced anaphylaxis in the FDA adverse reporting system (FAERS)[1] Another recent publication by Baker et al confirmed that biologics as a whole administered at home compared to those administered in a facility were associated with increased adverse events requiring escalation of therapy[2]. **The UHC policies do not adequately address safety or the adverse events of Xolair.** In fact, the only mention of adverse reactions to Xolair (Deschildre, et al) notes that 5.7% of patients discontinued Xolair due to "significant adverse events."[3]

Adherence

Another significant concern regarding self-administration at home, relates to adherence. It is clearly known that lack of adherence is a direct cause of poor healthcare outcomes. Self-administration at home is associated with decreased adherence. Poor handling and storage of delivered drug and non-adherence will lead to increased waste of these expensive medications. At-home delivery, storage, and self-administration poses a higher risk of non-adherence versus in-office administration where adherence can more easily be monitored. Medications obtained through the medical benefit and administered in the office are not paid for by the payor if the patient does not present for administration. Also, due to the nature and incentives of specialty pharmacies to ship medications to homes, many patients are currently receiving biologic medications that go unused, which further adds to rising healthcare costs.

Healthcare Disparities

Under-represented minorities already suffer from disproportionately poorer health outcomes. UHC's policy change would further advance these inequalities. Social determinates of health such as language, cultural beliefs, and educational level dramatically effect under-represented minority patients and healthcare outcomes. This policy will undoubtedly worsen the outcomes in under-represented minorities due to the challenges of maneuvering through the specialty pharmacy access, communication, arranging shipment and delivery, storage, and administration (instructions are only available in English). The burden placed on these patients will result in furthering the challenges and worsening outcomes putting under-represented minorities at even higher risks.

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[1] Yu R, Krantz M, Phillips E, Stone C. Emerging Causes of Drug – Induced Anaphylaxis: A Review of Anaphylaxis – Associated Reports in the FDA Adverse Event Reporting System (FAERS). J. Allergy Clin Immunol Pract 2021 Feb; 9(2): 819-892.e2

[2] Baker M, Weng Y, Fairchild R, et al. Comparison of Adverse Events Among Home – vs – Facility – Administered Biologic Infusions, 2007-2017 2021; 4 (6): e2110268.doi 10.1001/jamanetworkopen.2021.10268

[3] Deschildre A, Marguet C, Salleron J, et. al., Add-on omalizumab in children with severe allergic asthma: a 1-year real life survey. Eur Respir J. 2013 Nov;42(5):1224-33.

Preserving the patient-physician relationship and promoting shared-decision making would also be hindered by this policy.

We urge UHC to delay and amend these policies so that patients and their physicians may continue to determine the most appropriate care and delivery of these lifesaving biologic medications.

Sincerely,

Luz S. Fonacier, MD, FACAAI
President
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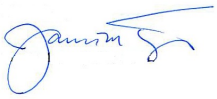

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