Product Description
Cosentyx® (secukinumab) is a human interleukin-IL-17A antagonist presented as 1) an injection in a single-use 150 mg/mL solution Sensoready pen 2) an injection in a single-use 150 mg/mL solution prefilled syringe, and 3) a lyophilized powder that is reconstituted for injection as a single-use 150 mg solution for healthcare professional use only.

Indications
Psoriasis
Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

Psoriatic Arthritis
Cosentyx is indicated for the treatment of adult patients with active psoriatic arthritis.

Ankylosing Spondylitis
Cosentyx is indicated for the treatment of adult patients with active ankylosing spondylitis.

Non-radiographic Axial Spondyloarthritis
Cosentyx is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.

Contraindication
In patients with a previous serious hypersensitivity reaction to secukinumab or to any of the excipients.

Cosentyx *is not indicated in other disease states. Please refer to the* Cosentyx *full prescribing information.*

[June 24, 2021]

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Dear Health Care Professional,

The COVID-19 pandemic has had a devastating impact on the global health care community. As of the date of this letter, interim results from phase 3 clinical trials for 5 COVID-19 vaccine candidates have been released.[1-6] Importantly, the United States Food and Drug Administration (US FDA) has issued emergency use authorizations (EUA) for 3 vaccine candidates for the prevention of COVID-19 caused by SARS-CoV-2. These EUA allow the distribution of the Pfizer/BioNTech COVID-19 vaccine candidate (BNT-162b2), the Moderna, Inc. COVID-19 vaccine candidate (mRNA-1273),and the Janssen Biotech, Inc. vaccine candidate (Ad26.COV2.S) in the United States.[7-9] These are important and exciting developments in the fight against this pandemic. However, data informing the efficacy and safety of these vaccine candidates in patients with immune-mediated diseases (IMIDs) receiving biologic therapies are limited.

Please know that Novartis is committed to providing you with information that may help you in making an informed clinical decision for your patients.

Overview – Vaccine Candidates

- According to the US Centers for Disease Control and Prevention, none of the vaccine candidates in phase 3 development use the live, attenuated SARS-CoV-2 virus to elicit an immune response.[10]

- mRNA vaccines: BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna)
    - These vaccines work through translation of mRNA to encode for the specific spike protein found on the surface of SARS-CoV-2 virus within the patient's myocytes. An immune response is elicited once the myocyte produces the specific spike protein and expresses it on its surface.[11,12]

- Replication-deficient viral vector vaccines: AZD1222 (AstraZeneca/Oxford) and Ad26.COV2.S (Janssen)
    - Vaccines consist of a replication-deficient adenoviral vector, which contains the SARS-CoV-2 spike protein gene. An immune response is then mounted once the specific spike protein is produced and expressed on the surface of the patient's own myocytes.[13,14]

- Protein-subunit vaccine: NVX-CoV2373 (Novavax)
    - Vaccine contains a recombinant SARS-CoV-2 nanoparticle constructed from the full-length wild-type SARS-CoV-2 spike protein. The vaccine adjuvant stimulates the entry of antigen-presenting cells into the injection site and enhances antigen presentation in local lymph nodes to enhance the immune response.[15]

- Phase 3 clinical studies evaluating the safety and efficacy of the SARS-CoV-2 vaccine candidates mentioned above employed the following exclusion criteria[14-18]:
    - Patients with any confirmed or suspected immunosuppressive or immunodeficient state
    - Patients receiving treatment with immunosuppressive therapy

What Does This Mean for Patients Taking Cosentyx® (secukinumab)? What Does the Current Vaccine Data Indicate?

- The US Prescribing Information for Cosentyx states that completion of all age appropriate immunizations according to current immunization guidelines should be considered prior to initiating therapy with Cosentyx. Cosentyx may alter a patient's immune response to live vaccines. **Avoid use of live vaccines** in patients treated with Cosentyx.[19]
- Healthy individuals who received a single, 150-mg dose of Cosentyx 2 weeks prior to vaccination with a non-US approved group C meningococcal polysaccharide conjugate vaccine and a non-US approved inactivated seasonal influenza vaccine had similar antibody responses compared to individuals who did not receive Cosentyx prior to vaccination. The clinical effectiveness of meningococcal and influenza vaccines has not been assessed within the Novartis sponsored clinical development program in patients with PsO (psoriasis), PsA (psoriatic arthritis), and axSpA (axial spondyloarthritis) undergoing treatment with Cosentyx.[19,20]
- A large observational study evaluating the immunogenicity of the Pfizer/BioNTech mRNA vaccine (BNT162b2) in adult patients with various autoimmune inflammatory rheumatic diseases (AIIRD), including PsA and axSpA, concluded that anti-cytokine biologics, including interleukin-17 inhibitors (IL-17i), can be continued in patients receiving the BNT162b2 mRNA vaccine. Details of this study are provided below.[21]
    - Furer et al. conducted a 6-week, prospective, observational, multicenter study to evaluate the immunogenicity of BNT162b2 in adult patients with AIIRD compared to the general population as

a primary outcome. Secondary outcomes included the effect of immunosuppressive treatments on vaccine immunogenicity, vaccine efficacy, vaccine safety, and the effect of the vaccine on disease activity.

- The study population included consecutive adult patients with various AIIRD (N=686) and a control group (N=121) without history of AIIRD and without immunosuppressive treatment.
- Immunogenicity was assessed 2-6 weeks following the second vaccine dose, based on serum IgG anti-trimeric S1/S2 spike glycoprotein antibodies. A value >15 binding antibody units (BAU) was considered as a cutoff of seropositivity.
- Of the 686 patients with AIIRD, 167 had a diagnosis of PsA and 74 had a diagnosis of axSpA. The seropositivity rate in patients with PsA and axSpA was 96.9% and 98.5%, respectively, compared to 100% in the control group.
- A total of 48 patients (40 with PsA and 8 with axSpA) were treated with an IL-17i.
- Almost 98% of patients (47/48; 97.92%) treated with an IL-17i had an appropriate immunogenic response (*P*=0.7529 vs controls). The seropositivity rate in patients receiving an IL-17i as monotherapy was 100% (37/37). In contrast, the seropositivity rate in patients receiving an IL-17i in combination with methotrexate was 85.71% (6/7).
- The prevalence of mild adverse events (AEs) was similar in AIIRD patients and controls. AEs of special interest in AIIRD patients were uveitis (n=2), herpes labialis (n=1), pericarditis (n=1), and herpes zoster (n=6). A total of 3 patients with AIIRD died after the 2nd vaccine dose. The background immunosuppressive therapy(ies) in these patients was(were) not specified.
- In patients with PsA and axSpA, post-vaccination indices of disease activity (PsA: DAPSA and PASI; axSpA: ASDAS) remained stable.
- The following limitations should be considered when interpreting the results of this study:
    - The authors did not specify which IL-17i agent(s) was(were) included in the analysis
    - Patients with AIIRD and control populations were not matched by age
    - Pre-vaccination COVID-19 antibody levels were not available
    - The analysis did not assess cellular immunity for seronegative patients

- Additional studies have described the use of BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), or AZD1222 (AstraZeneca) vaccines in patients with IMIDs, including psoriasis (PsO), PsA, and axSpA, treated with biologic disease-modifying antirheumatic drugs (DMARDs), including IL-17i.[22-27]
    - The conclusions from these studies were generally consistent with the Furer et al.[21] study described above. Overall, these studies suggest that while patients with IMIDs respond to SARS-CoV-2 vaccination, the responses may be reduced or delayed. Further, treatment with nonbiologic immunomodulators, such as methotrexate, appears to be associated with a reduced rate of adequate immunogenicity. In contrast, patients treated with anti-cytokine therapies, including IL-17i, appear to achieve similar levels of immunogenicity as healthy controls.
    - Detailed summaries are not provided as the sample sizes in these studies are limited and/or the studies are of lower standard of evidence (eg, case series/reports). Citations are provided for your reference.
- The American College of Rheumatology (ACR) COVID-19 Vaccine Clinical Guidance Task Force recommended (moderate level of consensus) that there should be no modifications to either the IL-17i therapy, including secukinumab, or the timing of the vaccination in relation to COVID-19 vaccine administration. Similarly, the National Psoriasis Foundation (NPF) COVID-19 Task Force recommended that patients receiving an mRNA-based or adenovirus vectored vaccine should continue their biologic for psoriasis (PsO) and/orPsA in most cases. The task force recommended shared decision-making between the clinician and patient to guide discussions about use of systemic therapies during the pandemic.[28-30]
- Non-Novartis sponsored studies have assessed the immunogenic response against seasonal influenza vaccines in PsA or ankylosing spondylitis (AS) patients undergoing treatment with Cosentyx. These studies indicate that secukinumab does not affect the humoral response to the seasonal inactivated influenza vaccine. Results are briefly summarized below.[31,32]

- Furer et al. evaluated the immunogenicity and safety of seasonal influenza vaccine in 32 PsA patients treated with secukinumab (median treatment duration: 13 months) vs 17 age- and gender-matched healthy controls. All participants received the Sanofi Pasteur 2017 vaccine, which contained the H3N3, H1N1, and B antigens. The authors concluded that secukinumab did not affect the humoral response to influenza vaccine in patients with PsA. The authors further noted that disease exacerbation was not observed following vaccination and no serious AEs were observed in either group.[31]
- Richi et al. assessed the immunological response to influenza vaccine in 17 patients with PsA or AS receiving secukinumab (mean treatment duration 8.9 months) vs 13 healthy volunteers. All participants were vaccinated with the seasonal inactivated trivalent influenza vaccine, containing the H1N1, H3N2, and B antigens. The authors concluded that secukinumab had no effect on the immunogenic response to the influenza vaccine with the proportion of responders being comparable between the groups.[32]

Professional Society Recommendations and Statements

- The ACR COVID-19 Vaccine Clinical Guidance Task Force has released the COVID-19 vaccine clinical guidance summary to provide guidance to rheumatology providers on the use of the COVID-19 vaccine and the associated management of patients with rheumatic diseases.[28]
  - Patients with rheumatic and musculoskeletal disease and AIIRDshould receive COVID-19 vaccination, consistent with the age restriction of the FDA approval (moderate level of consensus amongst task force panel).
  - COVID vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity (strong-moderate level of consensus amongst task force panel).
  - Beyond known allergies to vaccine components, there are no known additional contraindications to COVID-19 vaccination for AIIRD patients (moderate level of consensus amongst task force panel).
  - No modifications were recommended to either the IL-17i therapy, including secukinumab, or vaccination timing in patients with rheumatic musculoskeletal disease receiving a COVID-19 vaccine (moderate level of consensus amongst task force panel).
  - Patients with AIIRD are at a higher risk for hospitalized COVID-19 and worse outcomes compared to the general population (moderate level of consensus amongst task force panel).
  - Patients with AIIRD should be prioritized for vaccination before the non-prioritized general population of similar age and sex (moderate level of consensus amongst task force panel).
  - The expected response to COVID-19 vaccination for many AIIRD patients on systemic immunomodulatory therapies is likely to be blunted in its magnitude and duration compared to the general population (moderate level of consensus amongst task force panel).
  - A theoretical risk exists for AIIRD flare or disease worsening following COVID-19 vaccination. However, the benefit of COVID-19 vaccination for rheumatic and musculoskeletal disease patients outweighs the potential risk for new-onset autoimmunity (moderate level of consensus amongst task force panel).
  - The ACR guidance statements are part of a “living document” and will be updated when necessary. The full guidance document is available at: rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf

- The NPF COVID-19 Task Force has published guidance statements to promote optimal management of psoriatic disease during the pandemic, which include recommendations on what patients with psoriatic disease should do to protect themselves from becoming infected with SARS-CoV-2.[29,30]
  - NPF recommended that in most cases, patients should take the first COVID-19 vaccine currently approved by EUA for which they are eligible and offered based on federal, state, and local guidance. Systemic medications for PsO or PsA are not a contraindication to any currently available COVID-19 vaccines (be they mRNA-based or adenovirus vectored vaccine).
  - NPF also recommended that patients who receive an mRNA-based or adenovirus vectored vaccine COVID-19 vaccine continue their biologic or oral therapies for PsO and/or PsA in most cases. Shared decision-making between the clinician and patient was recommended to guide the discussion.
  - NPF indicated that decisions about the timing of latent tuberculosis infection (LTBI) screening to facilitate initiation of oral or biologic therapy should involve a risk-benefit discussion between individual patients and their prescribers until more data are available. The task force did not feel that there are enough data to raise concern for an interference between COVID-19 vaccines and tuberculin skin test/interferon gamma release assays results, and that for most patients, LTBI screening for biologic planning should proceed as planned, rather than be delayed.
  - The NPF guidance statements are part of a "living document” and will be updated when necessary. The full guidance document is available at: psoriasis.org/covid-19-task-force-guidance-statements/

[June 24, 2021]

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Additional Resources

For additional information related to the SARS-CoV-2 vaccines, please refer to the following:

- US Centers for Disease Control and Prevention: cdc.gov/coronavirus/2019-ncov/vaccines/index.html
- World Health Organization: who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines
- International Psoriasis Council. IPC Statement on SARS-CoV-2 Vaccines and Psoriasis: psoriasiscouncil.org/blog/IPC-Statement-on-SARS-CoV-2-Vaccines-and-Psoriasis.htm
- American College of Rheumatology. COVID-19 Clinical Guidance Summary for Adult Patients with Rheumatic Diseases: rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-Patients-with-Rheumatic-Diseases.pdf

For questions related to Novartis marketed products, please contact Novartis Medical Information at 1-888-NOW-NOVA (1-888-669-6682), Monday to Friday, 8:30 AM to 5:00 PM ET.

Finally, we want to express our deep gratitude for all you do every day for your patients and your communities. We are committed to doing all we can to support you during this time of need.

Sincerely,

Anthony Yadao, MD
Medical Unit Head, IHD
Immunology, Hepatology and Dermatology)

Antonio Martin, MD
Head of US Clinical Development and MedicalAffairs

Please see full Prescribing Information, including Medication Guide, available here:
https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/cosentyx.pdf

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