

# Ustekinumab (Stelara)

Ustekinumab is a biologic agent classified as an IL-12/IL-23 inhibitor. It was first approved by the U.S. Food and Drug Administration in 2009 for the treatment of moderate to severe plaque psoriasis. In 2013, it received additional approval for the treatment of psoriatic arthritis. This biologic is being investigated for use in various other immune-mediated inflammatory diseases, including Crohn's disease, sarcoidosis, and multiple sclerosis, due to its role in regulating immune responses that contribute to chronic inflammation.

## Mechanism of Action

Ustekinumab is a human monoclonal antibody. It functions by binding to the p40 subunit common to both IL-12 and IL-23 cytokines. This binding inhibits the activity of these cytokines, which play pivotal roles in the inflammatory response. IL-12 and IL-23 are integral to the differentiation and activation of T-helper cells (specifically Th1 and Th17 cells), which are involved in the pathogenesis of various inflammatory conditions. By blocking these cytokines, ustekinumab reduces the downstream effects of immune activation, thereby decreasing inflammation and tissue damage associated with diseases like psoriasis and psoriatic arthritis.

## Indications for Use

- **Chronic Plaque Psoriasis:** Ustekinumab is approved for the treatment of moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic or phototherapy. This form of psoriasis is characterized by the formation of raised, red, scaly patches on the skin, which result from the overactive immune system driving rapid skin cell turnover.
- **Psoriatic Arthritis:** Ustekinumab is approved for the treatment of psoriatic arthritis, either alone or in combination with methotrexate. Psoriatic arthritis is an inflammatory joint disease that occurs in individuals with psoriasis and is characterized by pain, stiffness, and swelling in the joints.
- **Investigational Uses:** Beyond its approved indications, ustekinumab is being researched for potential use in other inflammatory disorders, such as:
  - **Crohn's Disease:** A chronic inflammatory bowel disease that involves inflammation of the gastrointestinal tract.
  - **Sarcoidosis:** An inflammatory disease characterized by the formation of granulomas (clusters of immune cells) in various organs.
  - **Multiple Sclerosis:** A chronic autoimmune disease of the central nervous system that causes nerve damage and dysfunction.

## Side Effects and Safety Profile

As with all biologic therapies, ustekinumab carries a risk of side effects, although it is generally well tolerated. The most commonly reported side effects include:

- Nasopharyngitis: Inflammation of the nose and throat, often presenting as a cold.
- Upper Respiratory Tract Infections: Infections affecting the nose, throat, and sinuses.
- Headache and Fatigue: Common symptoms that can occur during treatment.
- Hypersensitivity Reactions: Including rash, itching, and in rare cases, more severe reactions like anaphylaxis.

In patients treated for psoriatic arthritis, common side effects include:

- Arthralgia: Joint pain not caused by inflammation.
- Nausea: An upset stomach, sometimes accompanied by vomiting.

A rare but serious side effect is reversible posterior leukoencephalopathy syndrome (RPLS), a condition that can cause neurological symptoms such as:

- Headache
- Seizures
- Confusion
- Visual disturbances

Ustekinumab, like other immunosuppressive biologics, may increase the risk of infections, including the reactivation of latent infections such as tuberculosis and hepatitis. Prior screening for tuberculosis is recommended before starting therapy, and patients should be monitored for signs of active infections during treatment. Additionally, ustekinumab may elevate the risk of malignancy, although this risk is still under investigation.

## Latest Treatment Advancements

The approval and use of ustekinumab have been a significant advancement in the treatment of autoimmune diseases, particularly psoriasis and psoriatic arthritis. Research is ongoing into its efficacy and safety in other conditions. New clinical trials are exploring its use in Crohn's disease and sarcoidosis, where its ability to regulate Th1 and Th17 cells may offer a new therapeutic approach for managing inflammation. Additionally, improvements in biologic therapy administration, such as subcutaneous injections with less frequent dosing, have increased patient adherence and convenience.

## Conclusion

Ustekinumab represents a promising therapeutic option for patients with moderate to severe psoriasis and psoriatic arthritis. By targeting key immune mediators involved in inflammatory processes, it reduces disease activity and improves patient quality of life. While generally well tolerated, its use requires careful monitoring for potential side effects, particularly infections and rare neurological events. Ongoing research into its use for additional inflammatory conditions further highlights its potential as a versatile treatment option in immunology.

## References

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