# SFDPH TB Clinic/UCSF TB-Targeted Immunotherapy Group (TB-TIG)* Recommendations for TB Screening in Persons taking Targeted Immunotherapies (including Tumor Necrosis Factor Inhibitors)

The use of new targeted immunotherapies (or biologics) has radically transformed the available treatment options for many chronic diseases. These targeted immunotherapies work by blocking specific molecules that mediate certain immune responses or by depleting the cells that express them. Some can also increase the risk of progression to active TB disease by downregulating the immunologic functions that contain TB organisms. This risk varies by drug class and mechanism of action[1].

The use of tumor necrosis factor (TNF)-alpha inhibitors has been associated with high risk of progression of TB; active TB infection occurring in the setting of TNF-inhibitor use has a greater likelihood of involving extra-pulmonary sites and of being disseminated at presentation compared with other TB cases[2]. The risk has been reported to be greater with infliximab and adalimumab than with etanercept[2]. Latent TB infection (LTBI) screening and treatment appears to significantly reduce the incidence of progression to active TB in these patients[3].

There is growing evidence that other targeted immunotherapies (e.g., PD-1/PDL-1 inhibitors, CTLA-4 inhibitors, JAK kinase inhibitors, and IL-6 and IL-23 inhibitors to name a few) are also associated with increased risk of TB reactivation. These targeted immunotherapies should be treated similarly as for a TNF-inhibitor. Data is rapidly emerging in this area as more targeted immunotherapies are approved. Based mostly on expert opinion, SFDPH recommends that patients with a diagnosis of LTBI should be initiated on treatment for at least 1 month, if possible, prior to starting those targeted immunotherapies where a risk for TB progression has been identified.

The Table lists targeted immunotherapies as of July 2023 where the manufacturer's package insert recommends TB testing[4]. This list may not include all available targeted immunotherapies; check the manufacturer's package insert for details.

**References**

1. Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2022. Available at URL: https://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/
2. Dixon WG, Hyrich KL, Watson KD, Lunt M, et al. Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register (BSRBR). Ann Rheum Dis. 2010;69(3):522.
3. Carmona L, Gómez-Reino JJ, Rodríguez-Valverde V, et al. Effectiveness of recommendations to prevent reactivation of latent tuberculosis infection in patients treated with tumor necrosis factor antagonists. Arthritis Rheum. 2005;52(6):1766.
4. List of targeted immunotherapies: Murrill MT, Velásquez GE, Louie J, Tahir P, Kim A, D. Szumowski JD, Salazar J, Minter D, Casalegno ML, Phillips A, Ernst J. Latent tuberculosis screening recommendations for targeted immunotherapies. Presented at the 2023 National Tuberculosis Conference. June 12, 2023, Atlanta, United States

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# Targeted Immunotherapies and TB Risk, 2023

University of California San Francisco TB Targeted Immunotherapy Group (TB-TIG)

TB testing with interferon-gamma release assay or tuberculin skin test is recommended for the following targeted immunotherapies (per the manufacturers drug insert)

| Drug Name | Mechanism/Target |
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| **Abatacept** | **Selective T-cell costimulation modulator, CTLA-4** |
| **Abrocitinib** | **Kinase inhibitor (JAK1)** |
| **Adalimumab** | **Anti-TNF-alpha mAb** |
| **Alemtuzumab** | **Anti-CD-52 mAb** |
| **Anakinra** | **IL-1 receptor antagonist** |
| **Baricitinib** | **Kinase inhibitor (JAK1/JAK2)** |
| **Brodalumab** | **Anti-IL-17 receptor mAb** |
| **Canakinumab** | **Anti-IL-1beta mAb** |
| **Certolizumab** | **Anti-TNF-alpha mAb** |
| **Deucravacitinib** | **Kinase inhibitor (TYK2)** |
| **Emapalumab** | **Anti-IFN-gamma mAb** |
| **Etanercept** | **Soluble TNF-alpha receptor** |
| **Golimumab** | **Anti TNF-alpha mAb** |
| **Guselkumab** | **Anti-IL-23 mAb** |
| **Inebilizumab** | **Anti-CD-19 mAb** |
| **Infliximab** | **Anti-TNF-alpha mAb** |
| **Ixekizumab** | **Anti-IL-17 mAb** |
| **Rilonacept** | **Soluble IL-1 receptor** |
| **Risankizumab** | **Anti-IL-23 mAb** |
| **Rituximab** | **Anti-CD-20 mAb** |
| **Ruxolitinib** | **Kinase inhibitor (JAK1/JAK2)** |

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| **Sarilumab** | **Anti-IL-6 receptor mAb** |
| **Satralizumab** | **Anti-IL-6 receptor mAb** |
| **Secukinumab** | **Anti-IL-17 mAb** |
| **Spesolimab** | **Anti-IL-36 receptor mAb** |
| **Tildrakizumab** | **Anti-IL-23 mAb** |
| **Tocilizumab** | **Anti-IL-6 receptor mAb** |
| **Tofacitinib** | **Kinase inhibitor (JAK1/JAK2/JAK3)** |
| **Upadacinitib** | **Kinase inhibitor (JAK1)** |
| **Ustekinumab** | **Anti-IL-12 and IL-23 mAb** |
| **Vedolizumab** | **Anti-integrin (a4B7) mAb** |

Abbreviations: CTLA-4, Cytotoxic T-lymphocyte associated protein 4; mAb, monoclonal antibody; TNF, tumor-necrosis factor; IL, interleukin; IFN, interferon

Note: While the manufacturers' package insert does not mentioned risk of active TB for the PD-1 (programmed cell death-1) and PDL-1 (programmed cell death ligand-1) inhibitor class of drugs, use in animal models has demonstrated increased severity of TB infections and enhanced inflammatory response. TB infected PD-1 knockout mice exhibit markedly decreased survival compared to wild-type controls, which correlated with increased bacterial proliferation and inflammatory responses in these animals. PD-1 blockage using a primate anti-PD-1 antibody was also shown to exacerbate TB infection in rhesus macaques. Pending further data, the SFDPH TB Clinic recommends TB testing prior to use of these classes of drugs (including atezolizumab, avelumab, cemiplimab, dostarlimab, durvalumab, nivolumab, nivolumab/relatlimab and pembrolizumab).