Introduction

Anser ADA, Anser IFX, Anser UST, and Anser VDZ testing are addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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What are Anser ADA, IFX, UST, and VDZ

Definition

The suite of Anser tests includes Anser ADA, Anser IFX, Anser UST, and Anser VDZ. All 4 tests measure serum concentrations of anti-drug antibodies in patients with diminished or suboptimal response to medications used to treat various inflammatory diseases.¹

Medications and Indications

Adalimumab (ADA), Infliximab (IFX), Ustenkinumab (UST), and Vedolizumab (VDZ) are monoclonal antibodies approved by the U.S. Food and Drug Administration (FDA) for use in various conditions:¹

- ADA: Crohn’s disease, ulcerative colitis, and rheumatoid arthritis
- IFX: Crohn’s disease, ulcerative colitis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis, and rheumatoid arthritis
- UST: active psoriatic arthritis
- VDZ: moderate to severe active ulcerative colitis or Crohn's disease
Loss of response

At the beginning of treatment, some patients exhibit an initial response to IFX, ADA, UST, and VDZ administration, yet experience loss of treatment response over time (secondary nonresponse). For example, the loss of clinical effect for infliximab for patients who have an initial therapeutic response is relatively common (loss of response [LOR], ranging from 3% to 13% per patient-year).

While the reasons for nonresponse among patients varies, research shows that anti-drug antibodies neutralize or increase during drug metabolism. It has also been hypothesized that it could be due to low serum levels of the medication, use of the drug in response to higher inflammatory disease burden, and development of immunogenicity.

Management options to loss of response include higher dosage of the drug, shorter intervals between drug doses, switching drugs, or any combination of the above. It has also been shown that the production of antibodies to either adalimumab or infliximab is associated with an increased rate of infusion reaction.

Anti-drug Antibodies

With the use of adalimumab, the development of anti-drug antibodies is correlated with reactions at the initial injection site, and infliximab-related anti-drug antibodies are correlated with acute infusion reactions and delayed hypersensitivity reactions. Infusion reactions have not been thoroughly evaluated with the use of vedolizumab-related or ustekinumab-related anti-drug antibodies.

Several assays are available for detection and measurement of circulating anti-drug antibody levels, including enzyme-linked immunoabsorbant assay (ELISA) (earlier generation technique), radioimmunoassay (RIA), and more recently, the homogeneous mobility shift assay (HMSA) offered by Prometheus (Prometheus Laboratories, Inc.) or the electrochemiluminescence immnosassay (ECLIA).

Test information

Introduction

Anser IFX, ADA, UST, VDZ are non-radiolabeled fluid-phase homogeneous mobility shift assays (HMSA) that measure the formation and serum concentrations of anti-drug antibodies in patients with diminished or suboptimal response to the inflammatory disease medications used to treat various inflammatory diseases: Infliximab (IFX; Remicade®, Janssen Biotech); Adalimumab (ADA; Humira®, AbbVie); Ustenkinumab (UST, Stelara®, Janssen Biotech, Inc.); and vedolizumab (VDZ; ENTYVIO®, Takeda Pharmaceuticals USA, Inc.). The formation of these ADAs may lead to patients who become nonresponsive to these various medications.
Guidelines and evidence

Introduction

This section includes relevant guidelines and evidence pertaining to Anser ADA, Anser IFX, Anser UST and Anser VDZ testing.

American Gastroenterological Association (AGA)

AGA Institute Guideline on Therapeutic Drug Monitoring (TDM) in Inflammatory Bowel Disease (2017) offered the following recommendation for measurement of anti-drug antibodies utilizing the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool:7

- “In adults with active IBD treated with anti-TNF agents, the AGA suggests reactive therapeutic drug monitoring to guide treatment changes. GRADE: Conditional recommendation, very low quality of evidence. The true effect is likely to be substantially different from the estimate of effect.”
- “In adult patients with quiescent IBD treated with anti-TNF agents, the AGA makes no recommendation regarding the use of routine proactive therapeutic drug monitoring. GRADE: No recommendation, knowledge gap.”

Literature review

The evidence is insufficient to support the use of the therapeutic drug monitoring with the Anser ADA, Anser IFX, Anser UST and Anser VDZ assays in patients with inflammatory conditions to guide treatment optimization with monoclonal antibodies. The overall benefit of therapeutic drug monitoring with Prometheus Anser assays has not been established.6,8-28

There is an absence of clinical utility studies evaluating if TDM-guided dosing adjustments leads to clinically meaningful changes in patient health outcomes, and how those outcomes compare with adjustments based on patient symptoms, clinical assessment, and conventional laboratory evaluation.

Well-designed studies are needed to expand the existing evidence base to confirm if TDM with ADA, UST, and VDZ leads to changes in therapeutic interventions or other changes in disease management that improve patient health outcomes over the long term. Studies should also report how these outcomes compare with adjustments based on patient symptoms, clinical assessment, and conventional laboratory evaluation.

Criteria

Introduction

Requests for Anser ADA, IFX, UST, and VDZ testing are reviewed using these criteria.
Criteria

- This test is considered investigational and/or experimental.
  - Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.
  - In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

References

Introduction

These references are cited in this guideline.

1. Promethius Anser. Integrated IBD Monitoring. Available at: https://www.anserifx.com/


