Title:	Anti-TNF drugs (Adalimumab, Infliximab, Etanercept) and anti-drug antibodies User Information
Subject:	Information for External Users

Version number	3
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Issued on	03/10/2022

Clinical Indications

Adalimumab, Infliximab and Etanercept are all drugs which inhibit the activity of tumour necrosis factor alpha (TNF-α). They are licensed for a number of clinical conditions, which include: Gastroenterology (Crohn's disease, ulcerative colitis), Rheumatology (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, juvenile idiopathic arthritis) and Dermatology (severe plaque psoriasis).

The measurement of anti-TNF drugs and their antibodies are useful tools in managing patients who fail to respond (primary non-response) or initial response followed by loss of response (secondary non-response) to treatment. Monitoring drug levels and anti-drug antibodies allows for a personalised approach to drug optimisation by appropriate dose escalation/de-escalation, drug switching/withdrawal, re-introduction after drug interruption, adherence to therapy or confirmation of drug reactions.

Patient preparation / other factors

Trough (pre-dose/pre-infusion) samples are recommended.

Specimen Type

Serum preferred (lithium heparin plasma also acceptable). Grossly haemolysed (>2 g/L haemoglobin) or icteric (>0.2 g/L bilirubin) samples are not suitable.

Volume required

Minimum 300 µL

Sample Handling

Centrifuge sample at 3000 rpm for 10 minutes, aliquot serum or plasma and store at 2-8°C until transport.

Storage Conditions

Samples should be stored at 2–8°C. If transport is to be delayed over 5 days please freeze samples at -20°C until dispatch by post.

Specimen Transport to Lab

1st Class Post

Address for Sample Transport

Send samples to:

Synnovis, Central Specimen Reception - Special Processing Unit

5th Floor, North Wing

St Thomas' Hospital

Westminster Bridge Road,

London SE1 7EH

Assays available (anti-TNF alpha) - Lisa-tracker ELISA assays

Infliximab (Remicade®)

Infliximab biosimilars: Inflectra™, Remsima™, Flixabi™

Adalimumab (Humira®)

Adalimumab biosimilars: Imraldi™, Amgevita™

Etanercept (Enbrel®)

Assays available but not in routine service (others)

The following assays are not currently in routine service however we hope to expand our repertoire to include them in the near future. In the meantime analysis can be arranged if required – please contact the laboratory to discuss.

Golimumab (Simponi®)

Vedolizumab (Entyvio®) (anti- α4β7 integrin)

Certolizumab Pegol (Cimzia®)

Ustekinumab (Stelara®) (anti-IL12/23 IgG1 kappa human monoclonal antibody)

Results line/reports

020 7188 8008 (Select option 1) / viapath.customersupport@nhs.net

Laboratory contacts for results discussion

Zehra Arkir (Consultant Clinical Scientist)

020 7188 1253 / Zehra.Arkir@gstt.nhs.uk

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UKAS Accreditation for: ISO 15189:2012- Medical Laboratories

Reference no: 9093

External Quality Control

Currently no suitable EQA schemes are available in the UK. Infliximab and Adalimumab drug and anti-drug antibody assays are subject to sample exchange and regular evaluation against other CE marked kits.

Therapeutic Ranges - guidance

Infliximab

Therapeutic drug levels	> 2.5 µg/mL
Intermediate drug levels	1.2 – 2.4 µg/mL
Sub-therapeutic drug levels	<1.2 µg/mL

Adalimumab

Levels of >6 µg/mL are considered adequate.

Etanercept

Therapeutic range for Etanercept has yet to be defined but a literature review of studies using our kits suggests Etanercept concentration of 3.1 µg/mL at 3 months predicts a response at 6 months.

Anti-drug antibody reference ranges

Anti-Infliximab antibodies - ≤10 ng/mL

Anti-Adalimumab antibodies - ≤10 ng/mL

Anti-Etanercept antibodies - ≤10 ng/mL

Please note, full interpretation requires complete clinical information: drug dosage/frequency, previous exposure to other biologics, time of sampling, duration of therapy and clinical assessment.

Turnaround Time

14 days. Urgent analysis can be arranged – please contact the laboratory to discuss.

Longer turnaround times may be experienced for Etanercept.

Additional Information/Interpretive comments

Analysis of free anti-drug antibody is provided as a reflex test where clinically indicated, i.e. when anti-TNFα drug result is in the sub-therapeutic range.

Anti-drug antibodies may be neutralising or non-neutralising depending on which part of the anti-TNF drug they are directed against (idiotype or non-idiotype). ELISA assays in routine clinical use are not capable of distinguishing neutralising from non-neutralising anti-drug antibodies. Both neutralising and non-neutralising antibodies will accelerate drug clearance leading to sub-therapeutic drug levels.

Tailored comments are added to all results and will depend on drug and antibody concentration, clinical history and previous results.

No known cross-reactivity with other antibodies or serum components including cryoglobulins, rheumatoid factor, heterophilic antibodies, triglycerides, bilirubin, IgG/IgM, C1q proteins and autoantibodies.