

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

Version number            2

Author                      Jenny Leung/Luisa Beltran

Authorised by              Zehra Arkir

Issued on                    07/02/2020

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### **Clinical Indications**

Adalimumab, Infliximab and Etanercept are all drugs which inhibit the activity of tumour necrosis factor alpha (TNF- $\alpha$ ). 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  $\mu$ L

### **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.

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**Specimen Transport to Lab**1<sup>st</sup> Class Post**Address for Sample Transport**

Send samples to:

Viapath, Central Specimen Reception - Special Processing Unit

5<sup>th</sup> 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-  $\alpha 4\beta 7$  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](mailto:viapath.customersupport@nhs.net)

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**Laboratory contacts for results discussion**

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Luisa Beltran (Principal Clinical Scientist)

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Jenny Leung (Senior Clinical Scientist)

020 7188 1264 / [Jenny.Leung@viapath.co.uk](mailto:Jenny.Leung@viapath.co.uk)**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 &gt;6 µg/mL are considered adequate.

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**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.

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