Symbol	EN	FR	ES	IT	DE	PT	HR	SV	NL
	Sufficient for <n> tests	Suffisant pour <n> tests	Suficiente para <n> pruebas	Sufficiente per <n> analisi	Inhalt ausreichend für <n> Prüfungen	Suficiente para <n> testes	Dostatno za <n> testova	Räcker till <n> tester	Voldoende voor <n> tests
	Read instruction for use	Veuillez lire les Instructions d'utilisation	Lea las instrucciones de uso	Leggere le istruzioni per l'uso	Gebrauchsanweisung beachten	Leia as instruções de uso	Pročitati upute za uporabu	Läs bruksanvisningen	Lees de gebruiksaanwijzing
	Use by Date	Date de péremption	Fecha de caducidad	Usare entro	Verwendbar bis	Validade	Upotrijebiti do datuma	Används senast datum	Gebruik voor Datum
	Batch code	Code du lot	Código de lote	Codice lotto	Chargenbezeichnung	Código de lote	Šifra serije	Lotnummer	Lotnummer
	Catalog number	Numéro de catalogue	Número de catálogo	Numero di catalogo	Katalognummer	Número do catálogo	Kataloški broj	Katalognummer	Catalogus nr.
	Caution	Attention	Precaución	Attenzione	Gebrauchsanweisung beachten	Atenção	Oprez	Försiktighet	Waarschuwing
	Manufacturer	Fabricant	Fabricante	Produttore	Hersteller	Fabricante	Proizvođač	Tillverkare	Fabrikant
	Importer	Importateur	Importador	Importatori	Importeur	Importador	Uvoznik	Importörernas	Importeur
	Authorized representative of the European Community	Représentant autorisé de la Communauté européenne	Representante autorizado en la Comunidad Europea	Rappresentante autorizzato nella Comunità Europea	Bevollmächtigter in der Europäischen Union	Representante autorizado da Comunidade Europeia	Ovlašteni predstavnik Europske zajednice	Behörig företrädare för Europeiskage menskapen	Bevoegde verte genwoordiger van de Europese Gemeenschap
	In vitro diagnostic medical device	Dispositif médical de diagnostic in vitro	Dispositivo médico de diagnóstico In vitro	Dispositivo medico-diagnostico in vitro	Bevollmächtigter in der Europäischen Union	Dispositivo médico para diagnóstico in vitro	In vitro dijagnostički medicinski uređaj	Medicinsk utrustning för in vitro-diagnostik	In vitro diagnostisch medisch hulpmiddel
	Temperature limit	Limite de température	Límite de temperatura	Limite di temperatura	Temperaturbegrenzung	Limite de temperatura	Temperaturni režim	Temperatur gräns	Temperatuur grens
	Do not reuse	Ne pas réutiliser	No reutilizar	Non riutilizzare	Nicht zur Wiederverwendung	Não reutilizar	Ne ponovno upotrijebiti	Återanvänd inte	Niet opnieuw gebruiken
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices	Ce produit est conforme aux exigences de la Directive 98/79/EC sur les dispositifs médicaux de diagnostic in vitro	Este producto cumple con los requisitos de la Directiva 98/79/EC sobre dispositivos de diagnóstico In vitro	Questo prodotto soddisfa i requisiti della Direttiva 98/79/CE sui dispositivi medici diagnostici in vitro	Dieses Produkt entspricht den Anforderungen der europäischen Richtlinie 98/79/EG über In-vitro-Diagnostika	Este produto cumpre os requisitos da Diretiva 98/79/CE sobre dispositivos médicos de diagnóstico in vitro	Ovaj proizvod ispunjava zahtjeve Direktive 98/79/EC o in vitro dijagnostičkim medicinskim uređajima	Denna produkt uppfyller kraven i direktiv 98/79/EG om medicintekniska produkter för in vitro-diagnostik	Dit product voldoet aan de vereisten van de Richtlijn 98/79/EG op in vitro diagnostisch medisch hulpmiddelen

Document No.: INS-FM_G-B-TO
Revision date: March 30, 2023 (Rev. 01)

ez-Tracker

Infliximab

Theradiag
14 Rue Ambroise Croizat 77183 Croissy Beaubourg France
Tel: +(33)-1-64-62-10-12, Fax: +(33)-1-64-62-09-66
www.theradiag.com

Boditech Med Inc.
43, Geodudanji 1-gil, Dongnae-myeon,
Chuncheon-si, Gang-won-do 24398, Republic of Korea
Tel: +(82)-33-243-1400, Fax: +(82)-33-243-9373
www.boditech.co.kr

Obelis s.a.
Bd. Général Wahis 53, 1030 Brussels, Belgium
Tel: +(32)-2-732-59-54, Fax: +(32)-2-732-60-03
mail@obelis.net

EN

ez-Tracker Infliximab

INTENDED USE

ez-Tracker Infliximab is a fluorescence immunoassay (FIA) for the quantitative determination of free infliximab in human whole blood/serum/plasma.

For *in vitro* diagnostic use only.

INTRODUCTION

Infliximab is a chimeric monoclonal antibody which has high specificity for TNFα[1]. The introduction of infliximab has innovated the treatment of chronic inflammatory diseases like inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, or psoriasis, etc., and approved by FDA. [2, 3]

The treatment with infliximab can only exert its pharmacological effect when adequate concentrations are achieved in the circulation.[4] The trough level is defined as the drug concentration in the blood measured right before the next infusions, and has been used for therapeutic drug monitoring (TDM).[5, 6] The study of the relationship between trough level and clinical response shown that a good clinical efficacy is correlated with the adequate trough concentrations in IBD [7] and RA [8, 9] patients. The monitoring of infliximab drug level in circulation could provide opportunities to help personalized dosing strategies in patients.

ez-Tracker Infliximab has been developed for the quantitative determination of the drug level of free infliximab in plasma, serum, and whole blood.

ez-Tracker Infliximab uses a pair of highly specific monoclonal antibodies, which shows that equal quantitative performance to infliximab (Remicade®) and the infliximab biosimilars, CT-P13 and SB2.

PRINCIPLE

ez-Tracker Infliximab uses a sandwich immunodetection method; the fluorescent and biotin labeled anti-infliximab antibodies in buffer bind to infliximab in the sample, forming drug-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized-streptavidin on the test strip.

The more infliximab in the sample will form more drug-antibody complexes which lead to stronger intensity of fluorescence signal, which is processed by the instrument for ez-Tracker tests to show infliximab concentration in the sample.

COMPONENT

ez-Tracker Infliximab consists of 'cartridges'.

- Each sealed aluminum pouch contains two cartridges.
- Each cartridge packaged in an aluminum pouch has three components including a cartridge part, a detector part, and a diluent part.
- The cartridge part contains the membrane called a test strip which has streptavidin at the test line, and chicken IgY at the control line.
- The detector part contains anti-infliximab-fluorescence conjugate, anti-chicken IgY-fluorescence conjugate, biotin anti-infliximab, mouse IgG, sucrose, and bovine serum albumin (BSA) as a stabilizer in phosphate buffered saline (PBS).
- The diluent part contains tween 20 and sodium azide as a preservative in phosphate buffered saline (PBS).

WARNING AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges. A cartridge should be used for testing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use a cartridge, if the pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- If test components and/or sample are stored in refrigerator, then allow cartridge and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ez-Tracker tests may generate slight vibration during use.
- Used cartridges, C-tips and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The cartridge contains sodium azide (NaN_3), and they may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- No Biotin interference was observed in **ez-Tracker Infliximab** when biotin concentration in the sample 200 ng/mL was below. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake.
- **ez-Tracker Infliximab** will provide accurate and reliable results subject to the below conditions.
  - **ez-Tracker Infliximab** should be used only in conjunction with the instrument for ez-Tracker tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
K_2 EDTA, Na_2 EDTA, Na citrate, Lithium heparin, Na heparin

- **C-tip should be used when the following conditions are met.**
  - C-tip provided with the kit is recommended to obtain correct test result.
  - Capillary blood should be immediately tested after collection.
  - Do not perform a test with C-tip on General Mode. It might cause an erroneous result.
  - Excess capillary blood around the C-tip should be wiped off.
  - In order to avoid cross-contamination, please do not re-use C-tip for multiple samples.
  - ez-Tracker cartridge should be inserted and positioned in the cartridge holder prior to the blood sample collection.
  - While collecting blood, be careful not to create air bubbles in the C-tip.

LIMITATIONS OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the drug to the antibodies which is the most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the drug with time and/or temperature may also cause false negative result as it makes the drug unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.

STORAGE AND STABILITY

	Storage condition		
Component	Storage Temperature	Shelf life	Note
Cartridge	2 – 30 °C	20 months	Unopened
		1 months	Resealed

- Return an unused cartridge to the spare cartridge zipper bag containing the desiccant pack. Reseal along entire edge of zip-seal.

MATERIALS SUPPLIED

REF ETI 002-24

Components of **ez-Tracker Infliximab**

Cartridge	CART	24
Pipette tip (Zipper bag)	P-T	24
C-tip (Zipper bag)	C-T	24
ID chip	ID-C	1
Spare cartridge zipper bag	SCZB	1
Instructions for use	IFU	1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ez-Tracker Infliximab.**

Please contact our sales division for more information.

- **ez-Track**[1] REF ET 001
- **ez-Traker Infliximab Control** REF ETI 002-C
- **ez-Traker Infliximab Calibrator** REF ETI 002-CAL

SAMPLE COLLECTION AND PROCESSING

The sample type for **ez-Tracker Infliximab** is human whole blood/serum/plasma.

- It is recommended to test the sample within 24 hours after collection.
- The samples (serum, plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The samples (serum, plasma) may be stored for a week at 2-8 °C prior to being tested. If testing will be delayed more than a week, samples (serum, plasma) should be frozen at -20 °C.
- The samples (serum, plasma) stored frozen at -20 °C for 1 month showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.
- Collection of capillary blood sample using C-tip

① Hold the C-tip horizontally and touch the surface of blood drop with the tip of the C-tip.

② Capillary action will automatically draw the blood sample to C-tip and stop.

③ Wipe off any excess blood around the tip.

④ Double-check if capillary blood is filled accurately in the C-tip and the instrument for ez-Tracker tests is ready for a test on the 'C-tip mode'.

TEST SETUP

- Check the components of the **ez-Tracker Infliximab** as described below: Cartridges, pipette tips, C-tips, an ID chip, a spare cartridge zipper bag and an instructions for use.
- If the sealed cartridge has been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.

EN

- Ensure that the lot number of the cartridge matches that of the ID chip.
- Turn on the instrument for ez-Tracker tests.
- Empty the tip box.
- Insert the ID chip into the 'ID chip port'.

※ **Please refer to the instrument for ez-Tracker tests operation manual for complete information and operating instructions.**

TEST PROCEDURE

General mode

1) Insert a cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Select the 'General mode' in the instrument for ez-Tracker tests.
4) Take 100 µL of the sample (whole blood/ serum /plasma/control) using a pipette and dispense it into the sample well of the cartridge.
5) Tap the 'Start' button on the screen.
6) The test result will be displayed on the screen after 10 minutes.

C-tip Mode

1) Insert a cartridge into the cartridge holder.
2) Take 30 µL of capillary blood using a C-tip.
3) Insert the capillary blood-filled C-tip into the tip hole of the cartridge.
4) Select the 'C-tip mode' in the instrument for ez-Tracker tests.
5) Tap the 'Start' button on the screen.
6) The test result will be displayed on the screen after 10 minutes.

INTERPRETATION OF TEST RESULT

- The instrument for ez-Tracker tests calculates the test result automatically and displays infliximab concentration of the test sample in terms µg/mL.
- Working range: 0.2-50 µg/mL
- Samples (serum, plasma) with infliximab concentration above 50 µg/mL can be diluted with saline (0.9 % NaCl in distilled water, not provided). The recommended dilution factor is 1:10.
  After dilution, multiply the result by the dilution factor. Please follow the below equation to obtain the final sample concentration.
  [Final sample conc. = Reported conc. X Dilution factor (10)]

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **ez-Tracker Infliximab**. For more information regarding obtaining the control materials, contact Theradiag's Sales Division for assistance.
  (Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**
  - Limit of Blank (LoB) 0.03 µg/mL
  - Limit of Detection (LoD) 0.12 µg/mL
  - Limit of Quantitation (LoQ) 0.20 µg/mL
- **High-dose Hook Effect**
  There is no high-dose hook effect at infliximab concentration up to 350 µg/mL.
- **Analytical specificity**
  - Cross-reactivity
    ez-Tracker Infliximab test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactivity materials	Concentration
Adalimumab	100 µg/mL
Etanercept	100 µg/mL
Golimumab	100 µg/mL

  - Interference
    Interferents listed in the following table were added to the test sample at the concentration mentioned below. **ez-Tracker Infliximab** test results did not show any significant interference with these materials.

Interference materials	Concentration
Hemoglobin	1,000 mg/dL
Bilirubin	40 mg/dL
Triglyceride	1,500 mg/dL
Rheumatoid factor	200 IU/mL
Human serum albumin	6 g/dL

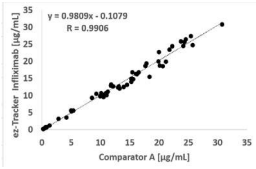
- **Precision**
  - Single-site study
    Repeatability (within-run precision)
    within-laboratory precision (Total precision)
    Lot to lot precision
    3 Lots of **ez-Tracker Infliximab** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.
  - Multi-site study
    Reproducibility
    1 Lot of **ez-Tracker Infliximab** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

Infliximab	Repeatability		Total precision	
[µg/mL]	AVG	CV (%)	AVG	CV (%)
2	2.00	4.0	1.98	4.6
10	9.66	5.8	9.85	4.9
20	19.09	5.6	19.09	5.5
Infliximab	Lot to lot precision		Reproducibility	
[µg/mL]	AVG	CV (%)	AVG	CV (%)
2	2.00	7.9	2.00	5.8
10	9.86	8.0	10.02	5.8
20	19.52	8.0	20.18	5.7

- **Accuracy**
  The accuracy was confirmed by testing with 3 different lots of **ez-Tracker Infliximab**. The tests were repeated 10 times at each concentration of the control standard.

Infliximab [µg/mL]	Lot 1	Lot 2	Lot 3	AVG	Recovery(%)
1.00	1.00	1.03	1.04	1.02	103
2.98	2.87	3.01	3.20	3.02	102
10.40	10.80	10.51	11.13	10.81	104
20.30	20.12	20.11	20.75	20.33	100
30.20	29.57	29.85	31.42	30.28	100
40.10	42.24	39.88	42.29	41.47	103

- **Comparability**
  Infliximab concentration of 55 clinical sample panels were quantified independently with **ez-Tracker Infliximab** and comparator A (ELISA) as per prescribed test procedures. Test results were compared, and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



REFERENCES

1. "Infliximab Use During Pregnancy". Drugs.com. 2 July 2019. Retrieved 13 August 2020.
2. "Infliximab, Infliximab-dyyb Monograph for Professionals". Drugs.com. American Society of Health-System Pharmacists. Retrieved 15 July 2019.
3. "Tumor necrosis factor inhibitors – state of knowledge." Arch Med Sci 2014; 10(6): 1175–1185.
4. "The impact of biologics on health related quality of life in patients with inflammatory bowel disease." Clin Exp Gastroenterol 2009;2:101-109.
5. "Assessing response and loss of response to biological therapies in IBD." Am J Gastroenterol 2011;106:685-698.
6. "New Trends in Inflammatory Bowel Disease." J Gastroenterol. 2015;22(3):103-111.
7. "Value of drug level testing and antibody assays in optimizing biological therapy." Frontline Gastroenterol 2013;4:41-43.
8. "Antibodies toward infliximab are associated with low infliximab concentration at treatment initiation and poor infliximab maintenance in rheumatic diseases." Arthritis Res Ther 2011;13:R105.
9. "Infliximab concentration monitoring improves the control of disease activity in rheumatoid arthritis." Arthritis Res Ther 2009;11:R178.