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-FN_G-B-TO
Revision date: March 30, 2023 (Rev. 01)

ez-Tracker

Anti-Infliximab Total Ab

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 Anti-Infliximab Total Ab

INTENDED USE

ez-Tracker Anti-Infliximab Total Ab is a fluorescence immunoassay (FIA) for the semi-quantitative determination of free and bound antibodies against infliximab in human serum/plasma.

For *in vitro* diagnostic use only.

INTRODUCTION

Monoclonal antibodies are now widely accepted as the biotherapeutic agent to treat several diseases.[1] The drug infliximab, a chimeric monoclonal antibody, has been marketed for several years in the United States and Europe for the treatment of chronic inflammatory diseases like inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, psoriasis, etc.[2,3] One of the major concerns, despite of its wide usage, is the potential development of antibodies to infliximab (ATI).[4,5] Furthermore, the ATI has interfered in infliximab efficacy and a significant number of patients lose their response to medication.[6] Finally, it can misleads the therapy by changing the treatment.[7, 8]

ez-Tracker Anti-Infliximab Total Ab used for a semi-quantitative detection of antibodies to infliximab (ATI) which can quantify both free and bound form. This method gives accurate and reliable determination of anti-infliximab antibody even in the presence of high infliximab concentration. Therefore, it is an ideal method for therapeutic drug monitoring. This assay is helpful for physician to accurate monitor and optimize the appropriate therapeutic strategy.

PRINCIPLE

ez-Tracker Anti-Infliximab Total Ab test uses a bridging immunoassay for detection of antibodies to infliximab. Sample is prepared by the dissociation and anti-infliximab antibodies from sample are bridged with fluorescent and biotin labeled infliximab which results in formation of an immune complex. This immune complex is migrated through nitrocellulose matrix and are captured by the immobilized streptavidin on the test strip.

The more antibodies to infliximab in the sample forms the more immune complex and leads to stronger intensity of fluorescence signal which is processed by the instrument for ez-Tracker tests to show anti-infliximab antibodies concentration.

COMPONENT

ez-Tracker Anti-Infliximab Total Ab consists of 'cartridges'.

- Each cartridge packaged in an aluminum pouch has four components including a cartridge part, a detector part, a liquid buffer part, and a dried buffer 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 infliximab-fluorescence conjugate, anti-chicken IgY-fluorescence conjugate, infliximab-biotin conjugate, mouse IgG, sucrose, bovine serum albumin, polyvinyl alcohol, polyethylene glycol, and bromophenol blue in tris-hydrochloride buffer.
- The liquid buffer part contains sodium azide as a preservative in glycine buffer.
- The dried buffer part contains L-Arginine, magnesium chloride, tween 20 and Pluronic F-68 in tris-hydrochloride buffer.

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 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 Anti-Infliximab Total Ab** 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 Anti-Infliximab Total Ab** will provide accurate and reliable results subject to the below conditions.
  - **ez-Tracker Anti-Infliximab Total Ab** will provide accurate and reliable results subject to the below conditions.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
K_2 EDTA, Na_2 EDTA, Sodium citrate

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 anti-drug antibody 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 anti-drug antibody 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 ℃	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 003T-24

Components of **ez-Tracker Anti-Infliximab Total Ab**

Cartridge	CART	24
Pipette tip (Zipper bag)	P-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 Anti-Infliximab Total Ab.**

Please contact our sales division for more information.

- **ez-Track[1]** REF ET 001
- **ez-Traker Anti-Infliximab Total Ab Control** REF ETI 003T-C
- **ez-Traker Anti-Infliximab Total Ab Calibrator** REF ETI 003T-CAL

SAMPLE COLLECTION AND PROCESSING

The sample type for **ez-Tracker Anti-Infliximab Total Ab** is human serum/Plasma.

- It is recommended to test the sample within 24 hours after collection.
- The samples (serum and plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The samples (serum and 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 should be frozen at -20 °C.
- The samples stored frozen at -20 °C for 1 month showed no performance difference.

TEST SETUP

- Check the components of the **ez-Tracker Anti-Infliximab Total Ab** as described below: Cartridges, pipette 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.
- 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.**

EN

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 (blood/serum/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 22 minutes.

INTERPRETATION OF TEST RESULT

- The instrument for ez-Tracker tests calculate the test result automatically and displays anti-infliximab concentration of the test sample in terms AU/mL
- Working range: 8 - 250 AU/mL
- The cut-off: 10 AU/mL

Range	Interpretation
≥ 10 AU/mL	Positive
< 10 AU/mL	Negative

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 Anti-Infliximab Total Ab**. 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) 1.25 AU/mL
  - Limit of Detection (LoD) 7.99 AU/mL
- **High-dose Hook Effect**
  There is no high-dose hook effect at anti-infliximab concentration up to 3,000 AU/mL.
- **Analytical specificity**
  - Cross-reactivity

  ez-Tracker Anti-Infliximab Total Ab 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
Anti-adalimumab antibody	1,000 ng/mL
Anti-etanercept antibody	1,000 ng/mL
Anti-golimumab antibody	1,000 ng/mL

  - Interference

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

Interference materials	Concentration
Hemoglobin	500 mg/dL
Bilirubin	20 mg/dL
Triglyceride	2,000 mg/dL
Rheumatoid factor	200 IU/mL
Human serum albumin	12 g/dL

- **Precision**
  - Single-site study

  Repeatability (within-run precision)
  within-laboratory precision (Total precision)
  Lot to lot precision

  3 Lots of **ez-Tracker Anti-Infliximab Total Ab** 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 Anti-Infliximab Total Ab** 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.

Anti-infliximab Total Ab [AU/mL]	Repeatability		Total precision	
	AVG	CV (%)	AVG	CV (%)
12	12.90	3.7	12.90	3.4
50	50.04	1.6	49.96	1.5
100	101.62	2.2	101.70	2.2

Anti-infliximab Total Ab [AU/mL]	Lot to lot precision		Reproducibility	
	AVG	CV (%)	AVG	CV (%)
12	12.96	3.4	11.94	5.5
50	49.89	1.7	50.16	6.0
100	101.59	1.8	99.37	6.0

- **Accuracy**

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

Anti-infliximab Total Ab [AU/mL]	Lot 1	Lot 2	Lot 3	AVG	Recovery (%)
34.00	34.26	35.52	34.17	34.65	101.9
58.00	59.52	58.03	57.03	58.19	100.3
106.00	103.57	106.79	109.87	106.74	100.7
154.00	153.56	154.63	154.73	154.31	100.2
202.00	203.66	205.58	199.14	202.79	100.4
226.00	220.68	233.12	230.74	228.18	101.0

- **Clinical performance evaluation**

  ez-Tracker Anti-Infliximab Total Ab has demonstrated the following clinical performance results.

Total (n=104)		n	ez-Tracker Anti-Infliximab Total Ab	
			Positive	Negative
Comparator A	Positive	25	23	2
	Negative	79	2	77
Positive Agreement (≥ 10 AU/mL)			92.0%	
Negative Agreement (< 10 AU/mL)			97.5%	
Total Agreement			96.1%	

REFERENCES

1. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med (2005) 353:2462–2476.
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. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet 2002; 359:1541–1549
5. Elliott MJ, Maini RN, Feldmann M, Long-Fox A, Charles P, Bijl H, et al. Repeated therapy with monoclonal antibody to tumour necrosis factor alpha (cA2) in patients with rheumatoid arthritis. Lancet (1994) 344:1125–7
6. Afif W, Loftus EV, Jr., Faubion WA, Kane SV, Bruining DH, Hanson KA, Sandborn WJ. Clinical utility of measuring infliximab and human anti-chimeric antibody concentrations in patients with inflammatory bowel disease. Am J Gastroenterol (2010) 105(5): 1133-1139
7. Colombel JF, Sandborn WJ, Reinisch W, et al. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med (2010) 362(15):1383–1395.
8. Peake ST, Bernardo D, Mann ER, Al-Hassi HO, Knight SC, Hart AL. Mechanisms of action of anti-tumor necrosis factor α agents in Crohn's disease. Inflamm Bowel Dis. (2013) 19:1546–1555.