Export Only Version

Erythrocytes Thiopurine Methyltransferase (TPMT) Activity Immunoassay

8-Patient Kit

REF **7018**

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BIOMERICA

I. INTENDED USE

The patented Biomerica TPMT activity assay is a competitive microwell immunoassay for the semi-quantitative determination of TPMT activity in erythrocytes. These reagents are for *in vitro* diagnostic use only.

II. SUMMARY AND EXPLANATION

TPMT (thiopurine methyltransferase) is a cytoplasmic enzyme that catalyzes the S-methylation of sulfhydryl compounds that include several thiopurine drugs such as thioguanine, azathioprine, and mercaptopurine. Thiopurine drugs may be used to treat:

a) Some types of leukemia and lymphoma;
b) Inflammatory bowel disease, including Crohn's disease and ulcerative colitis;
c) Autoimmune diseases, including rheumatoid arthritis and lupus;
d) Skin conditions, including psoriasis and eczema;
e) Rejection of organ transplants.

TPMT activity exhibits genetic polymorphism in the human population, and as a result of these genetic polymorphisms, a significant fraction of the population cannot metabolize these therapeutic drugs effectively. Approximately 90% of the population have no TPMT genetic changes, and can metabolize the drug in a predictable way. About 10% of people have one normal gene copy and one gene variant. These people can take the drugs but they metabolize these drugs more slowly, and may require lower doses to avoid side effects. A small number of people (approximately 1 in 300) have two gene variants, and thus have very low TPMT activity, or none at all. These people are at highest risk for side effects from the drugs, which can include damage to the bone marrow, resulting in a slow-down or cessation of white blood cell production. This can lead to infections, which can be life-threatening. Therefore measurement of TPMT activity levels is important in understanding drug metabolism, toxicity, and therapeutic efficacy.

III. PRINCIPLE OF THE TEST

The TPMT activity assay is a competitive microwell immunoassay for the semi-quantitative determination of TPMT activity in erythrocytes prepared from lysed red blood cells. TPMT catalyzes the S-methylation of 6-mercaptopurine (6-MP) with the presence of S-adenosylmethionine (SAM), the methyl donor, yielding 6-methylmercaptopurine (6-MMP). 6-MMP is then measured with a microwell EIA.

The Biomerica Microwell EIA is a competitive immunoassay. 6-MMP in the sample and 6-MMP conjugated with the enzyme compete for binding with its specific antibody. Antibody to 6-MMP is bound to a secondary biotinylated anti-rabbit antibody, which has been bound to a steptavidin-coated micoplate well. If little or no 6-MMP is present in the sample more enzyme labeled 6-MMP will bind to the anti-6MMP antibody bound to the solid surface. If a large or a significant amount of 6-MMP is present in the sample, less enzyme labeled 6-MMP will bind to the anti-6-MMP antibody, producing a lower color signal. The absorbance produced is inversely proportional to the amount of 6-MMP in the sample, calibrator or control. Using calibrators of known TPMT activities plotted against their response, the TPMT activity in the unknown samples can be quantified.

TPMT Activity Definition: One unit of TPMT is defined as a formation of 1 nmol of 6-MMP per ml of packed red blood cells per 60 min incubation at 37°C.

IV. KIT COMPONENTS

1. **6-MP SOL =** 6-MP Solution ..... 1 x 1.2 ml
2. **SAM =** S-Adenosylmethionine ..... ……. 1 x 2.0 mg
3. **SPE RXN BUF =** Specimen Reaction Buffer ..... 1 x 10 ml
4. **RXN STP SOL =** Reaction Stop Solution ..... 1 x 10 ml
5. **PLA 6-MMP AB=** 6-MMP Coated Antibody Plate .....4 strips
6. **CAL 1-6 =** Calibrators ..... 6 x 0.5 ml
   CAL 1: 0 U
   CAL 2: 3.75 U
   CAL 3: 7.5 U
   CAL 4: 15 U
   CAL 5: 30 U
   CAL 6: 60 U
7. **CTRL 1-2 =** Controls ..... 2 x 0.5 ml
   CTRL 1: Low Control <15 U
   CTRL 2: High Control >30 U
8. **CONJ ENZ 100X =** Enzyme Conjugate (100X).....1 x 0.040 ml
9. **EIA BUF =** EIA Buffer ..... 1 x 30.0 ml
10. **EIA STP SOL =** EIA Stop Solution ..... 1 x 20.0 ml
11. **BUF WASH 20X =** Wash Concentrate (20X) ..... 1 x 30.0 ml
12. **RGT B (TMB Subs) =** TMB Substrate Solution..... 1 x 20.0 ml

STORE ALL KIT COMPONENTS AT 2 – 8°C

MATERIAL AND EQUIPMENT REQUIRED BUT NOT PROVIDED:

1. Microplate reader
2. Microplate washer (Manual washing is acceptable)
3. Pipettes capable of dispensing volume of 10 to 1000 µL
4. Multichannel pipette or Eppendorf repeater pipette recommended
5. Graduated cylinders: 1000 mL
6. Disposable transfer pipettes
7. Distilled or reagent grade water
8. Saline (0.9% w/v NaCl)
9. Centrifuge capable of centrifuging at 13,000g
10. 37°C water bath
11. 2-8°C refrigerator
12. Ice or freezer
13. 1.5 ml micro-centrifuge tubes and holder
14. Parafilm or appropriate ELISA plate cover
15. 12x75 mm glass tube for preparing calibrators and samples for ELISA

16. Appropriate size container for working conjugate (Glass is acceptable)
17. Appropriate size container for working wash buffer
18. Vortex mixer
19. Timer

V. WARNINGS AND PRECAUTIONS FOR USERS

- **Important: Do not deviate from the specified procedures when performing this assay**. All dilutions, incubation times/temperatures and washings have been optimized for the best performance. Deviations from the specified procedures may affect the sensitivity and specificity of the assay.
- **Important: Adherence to the sample processing procedure is of extreme importance to the successful running of this assay. Refer to Section VI.**
- All reagents are for *In Vitro* Diagnostic Use Only.
- Reagents from different kit lots should not be interchanged.
- Do not use reagents that are beyond their expiration dates.
- All reagents should be at room temperature before using.
- The TMB substrate solution should not be exposed to strong light during storage or incubation. Ensure that the reagent is colorless before using.
- Wear gloves when performing the test, and handle specimens and used microwells as if able to transmit infectious agents.
- Treat all reagents and samples as potentially infectious materials. Use care to prevent aerosols and decontaminate any sample spills.
- Avoid contact with EIA Stop Solution. Stop solution is 1N HCl. In case of contact with skin or mucous membranes, flush with water immediately.
- Some reagents in this kit contain sodium azide as a preservative. Sodium azide may react with lead and copper plumbing to form explosive metal azides. When disposing of these reagents, always flush with large volumes of water to prevent azide build-up.
- Although the reagents provided in this kit have been specifically designed to contain no human blood components, the human patient samples, which might be positive for HBsAg, HBcAg, or HIV antibodies, must be treated as potentially infectious biohazards. Common precautions in handling should be used as normally applied to any untested patient sample.

VI. SPECIMEN COLLECTION AND STORAGE

An ideal specimen is venous blood collected in an EDTA tube. Specimens should be shipped to a testing laboratory while stored at 2-8°C via Next-Day delivery. Blood specimens should not be frozen. Frozen and/or hemolyzed specimens should be rejected.

Upon receipt in the laboratory, process the specimens within **24 hours** per the procedure outlined in **Section X**.

Important: Samples MUST be processed within 72 hours from the time of the blood draw. Ensure that the blood specimens are stored at 2-8°C prior to processing.

VII. RED BLOOD CELL AND LYSATE STORAGE

Whole blood sample can be immediately assayed following the sample processing procedure in **Section X**. However, if the ELISA test is not going to be run for at least 8 hours after lysing (Refer to **Section X)** the washed reconstituted RBCs may be stored at -70°C for up to 14 days.

For sample storage, it is recommended to aliquot 100µl of the washed reconstituted RBCs into a micro-centrifuge tube and store at –70°C. When needed thaw the frozen RBCs and directly add 400µl of ice-cold water to the tube for lysing. The frozen red blood cells **MUST** be completely thawed before proceeding. Thaw frozen red blood cells at 2-8°C. One hour at 2-8°C is adequate time for thawing frozen red blood cells.

Important: Red blood lysate cannot be frozen at –70°C. Only the reconstituted RBCs prior to lysing can be stored at –70°C.

VIII. REAGENT PREPARATION AND STORAGE

SAMPLE PROCESSING REAGENTS

Specimen Reaction Buffer and Reaction Stop Solution: Ready to use. No additional dilution or preparation needed. Let the reagent come to room temperature prior to using. The solution is stable up to the expiration date indicated on the vial when stored at 2-8°C.

SAM Solution: S-Adenosylmethionine (SAM) is provided as 2.0 mg powder. Add 1.8 ml distilled or deionized water to dissolve the powder completely before use. The solution is stable at room temperature (23 ± 4°C) for 5 hours.

6-MP Solution: Ready to use. No additional preparation needed. The 6-MP solution may become solid upon refrigerated storage but will dissolve upon warming at 37°C per **Step 3** of the methylation reaction section in the sample process (**Section X)**. This reagent is stable up to the expiration date indicated on vial label when stored at 2-8°C.

Saline Solution (0.9% w/v NaCl): Not Provided in Kit. To prepare saline solution, add 9 grams NaCl to 1 L distilled or deionized water. Mix until dissolved. Make this reagent fresh prior to use.

ELISA REAGENTS

6-MMP Antibody Coated Plate: Ready to use. Allow plate to come to room temperature prior to use. Return any unused wells to the foil pouch with desiccant. Reseal pouch tightly to exclude moisture. The plate is stable up to the expiration date indicated on the plate label.

Calibrators and Controls: Refer to **Section IX** for preparation.

EIA Buffer, EIA Stop Solution, and TMB Substrate Solution: Ready to use. No additional dilution or preparation needed. Let the reagent come to room temperature prior to using. The solution is stable up to the expiration date indicated on the vial when stored at 2-8°C.

Working Wash Solution: Mix 30 ml of the 20X Wash Concentrate with 570 ml of deionized or distilled water to make the Working Wash Solution. Store the Working Wash Solution at room temperature. The Working Wash Solution is stable at room temperature (23 ± 4°C) for one month (31 days).

Working Enzyme-Conjugate: The conjugate concentrate has a titer of 1:100. For example, the working Enzyme-Conjugate is prepared by mixing 26µl of the Enzyme-Conjugate concentrate with 2574µl of the EIA Buffer. This is plenty of working conjugate for a four-strip assay. The concentrate is stable up to the expiration date indicated on the label when stored at 2-8°C.

Important: The working Enzyme-Conjugate MUST be prepared fresh for each assay. Refer to Step 5 in Section XI of the ELISA Procedure. Prepare conjugate no more than 10 minutes prior to adding to plate.

IX. PREPARATION OF PATIENT SAMPLE, CALIBRATORS, AND CONTROLS FOR ELISA ASSAY

Dilute calibrators, controls, and lysate sample 1:5 in EIA Buffer. For example, take 50µl of calibrators, controls, and processed lysate sample and add to 200µl of EIA Buffer. Mix thoroughly prior to use.

Important: Make calibrators and controls fresh for each assay. Prepare the diluted calibrators, controls and samples no more than 10 minutes prior to plating the assay (Refer to Step 4 in Section XI for ELISA procedure).

X. SAMPLE PROCESSING

RBC Lysate Preparation

*It is recommended to place distilled or deionized water in an ice-bath or freezer for cooling prior to starting the sample processing procedure below. The ice-cold water will be used for lysing as indicated in **Step 11**.*

1. Centrifuge **1 ml** of blood in a micro-centrifuge tube at 3,000g for **3 minutes** at room temperature.
2. Discard the plasma and the buffy coat on top of the red blood cells (RBCs).
3. Add **750µl** saline (0.9% NaCl, not provided in the kit, refer to **Section VIII** for preparation) and mix the RBCs by up-down pipetting using a transfer pipette.
4. Centrifuge the RBCs in saline at 3,000g for **3 minutes** at room temperature.
5. Carefully remove and discard the supernatant. Try not to disturb the packed RBCs.
6. Repeat steps 3 – 5 two more times for a total of three washes.
7. Set the last centrifugation at 10,000g and spin for **10 minutes**.
8. Carefully remove and discard all the supernatant. Try not to disturb the packed RBCs.
9. Add **75µl** saline solution (0.9% NaCl) to the packed RBCs in **Step 8**. With a transfer pipette mix thoroughly by up-down pipeting.

*NOTE: If the test is not going to be performed in the next 8 hours, the reconstituted RBCs may be stored at -70°C for up to 14 days. Refer to **Section VII** for storage procedure of washed RBCs.*

10. Using a standard 100µl pipette tip slowly draw and transfer **100µl** of the reconstituted RBCs from **Step 9** into a clean 1.5 ml micro-centrifuge tube. Reverse pipetting is recommended for transfer of the reconstituted RBCs.

NOTE: Ensure that before adding the reconstituted RBCs to the tube that the RBCs suspension is thoroughly mixed. It is recommended that the reconstituted RBCs are immediately mixed prior to transferring into the clean micro-centrifuge tube. Mix by up-down pipetting using a transfer pipette.

11. Add **400µl** of ice-cold distilled or deionized water to the reconstituted RBCs in **Step 10**.
12. Vortex the tube for **30 seconds**.
13. Incubate the tube at **2-8°C** for **30 minutes**.
14. Vortex the tube for **15 seconds** to ensure complete lysing of RBCs.
15. Centrifuge the RBC lysate at 13,000g for **10 minutes** at room temperature.
16. Carefully transfer **50µl** of the top supernatant liquid for testing into a clean 1.5 ml micro-centrifuge tube. It is often difficult to see where the supernatant ends and the membrane pellet begins so be careful not to aspirate the red cell membrane pellet when removing the supernatant for testing. Proceed to the methylation reaction.

NOTE: RBC lysate is stable at 2-8°C within 8 hours of preparation.

Methylation Reaction

Important: No more than 8 samples should be processed in one batch during the methylation reaction. If more than 8 samples are to be tested the samples should be split into a maximum of an 8 sample batch. It is recommended to run the batches consecutively, spacing each batch a few minutes apart.

1. Add **50µl** Specimen Reaction Buffer (SPE RXN BUF) to the 50µl lysate sample in **Step 16**.
2. Vortex the tube for **10 seconds**.
3. Pre-Incubate the micro-centrifuge tube containing the reaction buffer and lysate from **Step 1** in a **37°C** water bath for **20 minutes**. Pre-Incubate the 6-MP Solution in a **37°C water bath** for **20 minutes** (**Refer to Section VIII).**

NOTE: A water bath set at 37°C should only be used. It is not recommended to use a standard incubator for the methylation reaction. Ensure the temperature of the water bath is 37°C prior to starting incubation.

4. Vortex the 6-MP Solution for **3 seconds**.
5. Add **15µl** 6-MP Solution to the tube.
6. Add **15µl** prepared SAM Solution (**Refer to Section VIII)** to the tube.
7. Vortex the tube after the addition of the SAM solution for **5 seconds**.
8. Incubate the tube in a **37°C** water bath for exactly **60 minutes**.
9. Add **50µl** Reaction Stop Solution (RXN STP SOL) to the tube.
10. Vortex the tube for **5 seconds**.
11. Allow the reaction mix to sit at room temperature for **30 minutes** prior to diluting for ELISA.
12. This reaction mix will be used in the subsequent assay procedure (**Section XI**).

Important: The reaction mix needs to be assayed within 1 hour.

XI. ELISA PROCEDURE

1. Allow all ELISA kit reagents to come to room temperature (23 ± 4°C).
2. Prior to starting the assay prepare the Working Wash Solution as stated in **Section VII**.
3. Place sufficient 6-MMP antibody coated microwell strips into a holder to run all six (6) 6-MMP calibrators (CAL 1- CAL 6), Control 1 and 2, and all patient samples.

NOTE: Run all Calibrators, Controls, and Patient Samples in duplicate.

4. Prepare diluted calibrators, diluted controls, and diluted processed lysate samples at the same time. Refer to Section IX. **Ensure to prepare diluted calibrators, controls, and samples no more than 10 minutes prior to plating.**
5. Prepare Working Enzyme-Conjugate (1:100) solution as stated in Section VII. **Ensure to prepare working conjugate no more than 10 minutes prior to adding to plate**.
6. Add **50µl** of the 1:5 dilution of the calibrators, controls, and patient samples into the designated or appropriate wells. Ensure to vortex the diluted samples prior to plating.
7. Add **50µl** of the Working Enzyme-Conjugate (1:100) to all wells. Cover the wells with parafilm or an appropriate microplate cover.
8. Incubate the wells at room temperature for **30 minutes**.
9. Wash each well 5 times with 300 µl of Working Wash Solution. After washing, completely remove any residual liquid in the wells by slapping the plate onto a dry paper towel until no liquid comes out.

NOTE: If washing manually decant the contents of the assay wells. Wash each well using the working wash solution in a squirt bottle with a fine-tipped nozzle, directing the wash solution to the bottom of the well with force. Fill the well, and then decant the wash solution out of the well. Repeat this step four more times for a total of five washes.

10. Add **100µl** of TMB Substrate Solution to all wells.
11. Cover the wells and incubate at room temperature **in the dark** for **30 minutes**. Place wells in a dark area or cover plate with aluminum foil.
12. Add **50µl** EIA Stop Solution to each well.
13. Read results within **five minutes** on a spectrophotometer having the wavelength set at 450 nm.

XII. CALCULATION OF RESULTS

Automated Method
Use an automated regression program to reduce the data, acceptable results will be obtained by using (1) Point to Point, or (2) 4 Parameter. Interpolate the patient values from the calibration curve**.** The lysate for a specimen with more than 60U may be diluted with Calibrator 1 (0 U) for further Testing.

Manual Method
Determine the mean absorbance for each calibrator, control, and sample.

- Construct a dose response curve where the average absorbance for each calibrator is plotted against the concentration of the corresponding calibrator (Refer to calibrator vial for concentration) on a semi-log or linear graph paper. Draw a straight line between 2 adjacent points. This mathematical algorithm is commonly known as the "point-to-point" calculation.
- Read off sample concentrations directly from the curve.

Any sample reading greater than Calibrator 6 (60 U) should be further diluted with Calibrator 1 (0 U) and reassayed.

XIII. QUALITY CONTROL

Both the high and low controls must be run with the test.

If the following quality control acceptance criteria are satisfied, the assay is valid:
The OD of the Low Control is greater than the OD of Calibrator 4 (15 U).

The OD of the High Control is lower than the OD of Calibrator 4 (15 U).

XIV. INTERPRETATION OF RESULTS

Human TPMT activity levels vary significantly, even in the population that has no known genetic deficiency. According to literature and current clinical practice, we have provided the following SUGGESTED result interpretation guide for your reference. It is the clinicians' and researchers' responsibility to interpret the results. Therapeutic decisions and research conclusions can NOT be made based on the following reference values.

< 7 Unit:	Very Low TPMT Activity Level, indicating a possible Homozygous Deficiency genomic type, approximately 0.3% of the human population.
7-17 Unit:	Medium TPMT Activity Level, indicating a possible Heterozygous Deficiency genomic type, approximately 11% of the human population.
> 17 Unit:	Normal to High TPMT Activity Level, indicating a possible Wild Type (normal) genomic type, approximately 89% of the human population.

Each Laboratory is encouraged to establish its own "Normal" and reference ranges based on populations encountered. These are suggested ranges, based on in-house studies at Biomerica, Inc.

XV. PERFORMANCE CHARACTERISTICS

Clinical Evaluation
Twenty Five whole blood samples were tested on the Biomerica TPMT test and a reference TPMT LC-MS/MS test. Linear regression shows the following association:

Biomerica TPMT ELISA = 1.05 TPMT LC-MS/MS – 6.35
pearson r = 0.923 N = 25

Sensitivity
The sensitivity, or minimum detection limit, of this assay is defined as the smallest single value, which can be distinguished from zero at the 95% confidence limit. The Biomerica TPMT ELISA has a calculated sensitivity of 0.80 U.

Precision and Reproducibility
Intra- Assay precision: Using control samples
The Intra-assay precision of the Biomerica TPMT ELISA Test was calculated from 25 replicate determinations on each high and low control sample.

Control Sample	Mean Value (U)	N	Coefficient of Variation %
1	5.9	25	8.72
2	45.8	25	5.32

Intra- Assay precision: Using patient samples
The Intra-assay precision of the Biomerica TPMT ELISA Test was calculated from 24 replicate determinations on three patient samples.

Patient Sample	Mean Value (U)	N	Coefficient of Variation %
1	26.1	24	4.80
2	12.1	24	9.43
3	9.2	24	10.29

Total Inter-Assay precision
The total precision (inter-assay variation) of the Biomerica TPMT ELISA Test was calculated from data on two samples obtained in 22 different assays, by five technicians on two different lots of reagents, over a two month period.

Sample	Mean Value (U)	N	Coefficient of Variation %
1	6.2	22	8.3
2	46.4	22	4.0

Inter-Assay Precision: Sample Preparation
Whole blood from eight patient samples was processed five separate times. Precision results are shown below:

Patient Sample	Mean Value (U)	Coefficient of Variation %
1	21.60	4.8%
2	21.16	6.8%
3	22.99	6.3%
4	14.46	10.7%
5	22.29	4.4%
6	20.44	3.6%
7	27.17	5.9%
8	21.43	7.4%

Inter-Assay Precision: Blood Draw
Whole blood from six patient samples was drawn at three separate time intervals and tested on the Biomerica TPMT ELISA, over two lots of reagents. Precision results are shown below:

Patient Sample	Mean Value (U)	Coefficient of Variation %
1	23.0	7%
2	26.9	7%
3	14.5	9%
4	20.7	5%
5	21.4	6%
6	21.6	6%

Linearity of Patient Sample Dilutions: Parallelism
Four patient samples were diluted with EIA Buffer. Results are shown below:

Sample	Dilution	Expected	Observed	% Observed/Expected
A	Undiluted	44.4		
	1:2	22.2	21.9	99%
	1:4	11.1	10.3	93%
	1:8	5.55	4.98	90%
B	Undiluted	27		
	1:2	13.5	13.4	99%
	1:4	6.75	6.1	90%
	1:8	3.375	3	89%
C	Undiluted	31.4		
	1:2	15.7	15.7	100%
	1:4	7.85	6.6	84%
	1:8	3.925	3.6	92%
D	Undiluted	30.2		
	1:2	15.1	14.9	99%
	1:4	7.55	6	79%
	1:8	3.775	3.1	82%
			AVERAGE	91%

Cross-reactivity
The following compounds, structurally and/or clinically related to 6-MMP, were tested for their cross-reactivities to the anti-6-MMP antibody at concentrations up to 10,000 ng/ml. The results were as follows:

	Spiked Conc. (ng/ml)	6-MMP Equivalent (ng/ml)	% Cross Reactivity
6-MMP	100	100	100%
6-MP	10,000	<2.5	<0.025%
Thioguanine	10,000	<2.5	<0.025%
Azathiopurine	10,000	<2.5	<0.025%

Interference

Sixty-seven (67) compounds, many of them commonly prescribed medicines and abused drugs, were selected for the study. A concentration of 10 µg/ml of each compound was found to have no positive or negative interference with the assay.

Acetaminophen	Ibuprofen
(5)-Acetylmorphine	Imipramine
Acetylsalicylic Acid	Isoxsuprine
(4)-Aminophenyl Sulfone	Ketamine
Amobarbital	Lidocaine
Ampicillin	Loperamide
Atenolol	Meperidine
Atropine	Mephentermine Hemisulfate
Benzoylecgonine	Methadone
Butabarbital	Nalbuphine
Chlordiazepoxide	Nalorphine
Chlorpromazine	Naproxen
Clonazepam	Niacinamide
Clorazepate	Norcocaine
Cocaethylene	Nystatin
Cocaine	Oxycodone
Codeine	Oxymorphone
(-)-Cotinine	Phencyclidine
Diacetylmorphine	Penicillin
Diazepam	Pentobarbital
Diphenhydramine	Phenylalanine
Ecgonine HCl	Phenylephrine
Ecgonine Methyl Ester	(beta)-Phenylethylamine
Fenfluramine	para-Methoxyamphetamine
Fenoprofen	para-Methoxymethamphetamine
Fluoxetine	Procainamide
Gemfibrozil	Procaine
Gentisic Acid	Propranolol
Glipizide	Quinidine
Heroin hydrochloride	Ranitidine
Hydrochlorothiazide	Salbutamol
Hydrocodone	Tolmetin
Hydromorphone	Zomepirac
Hydroxybenzoylecgonine	Δ9-Tetrahydrocannabinol

XVI. REFERENCES

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2. Deininger M, Szumlanski CL, Otterness DM, Van Loon J, Ferber W, Weinshilboum RM. Purine substrates for human thiopurine methyltransferase. Biochem Pharmacol. 1994 Nov 29;48(11):2135-8.
3. Indjova D, Shipkova M, Atanasova S, Niedmann PD, Armstrong VW, Svinarov D, Oellerich M. Determination of thiopurine methyltransferase phenotype in isolated human erythrocytes using a new simple nonradioactive HPLC method. Ther Drug Monit. 2003 Oct;25(5):637-44.
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XVII. SYMBOLS

	Storage Temperature
	Lot Code
	Expiration
	Manufacturer
	Authorized Representative
	Caution, see instructions
	For in vitro diagnostic use
	Catalog No.

XVIII. ORDERING INFORMATION

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