BIOSYNEX
Easy Diagnostics for Life

INSTRUCTIONS OF USE
URITOP+®

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1. INTENDED USE

Reactive strips for urine analysis URITOP+ are rigid plastic strips on which several areas of reagents are fixed. The test is intended for the qualitative and semi-quantitative detection in huan urine of one or more parameters : Urobilinogen, Glucose, Bilirubin, Ketones (Acetoacetic Acid), Specific Gravity, Blood, pH, Protein, Nitrite, Leukocytes, Ascorbic Acid, Microalbumine and Creatinine.
The test is intended for the diagnosis *in vitro* to professional use only.
Refer to the table below for the analyte as product references :

Name of the product	Ref	Parameters
URITOP+ 1	**1040003**	Glucose
URITOP+ 2	**1040004**	Glucose, protein
URITOP+ 3	**1040005**	Glucose, protein, pH
URITOP+ 4	**1040006**	Glucose, blood, protein, pH
URITOP+ 5	**1040007**	Glucose, ketones, blood, protein, pH
URITOP+ 7	**1040008**	Glucose, specific gravity, blood, leukocytes, protein, nitrites, pH
URITOP+ 10	**1040009**	Glucose, bilirubine, ketones, specific gravity, blood, leukocytes, protein, urobilinogen, nitrites, pH
URITOP+11	**1040010**	Glucose, bilirubine, ketones, specific gravity, blood, leukocytes, protein, urobilinogen, nitrites, pH, ascorbic acid
URITOP+13	**1040011**	Glucose, bilirubine, ketones, specific gravity, blood, leukocytes, protein, urobilinogen, nitrites, pH, ascorbic acid, microalbumine and creatinine

2. TEST PRINCIPLE

Urine undergoes many changes during the stages of disease or body dysfunction before blood composition is affected significantly. Urine analysis is a useful procedure indicator of good health or disease and is part of a medical database. Reactive strips can be used in a general health examination and allow the diagnosis and monitoring of systemic and metabolic diseases that affect kidney function, endocrinological diseases and diseases or disorders of the urinary tract infection.
Strips may be read visually by comparison of test paper attached to the plastic strip with the color chart blocks printed on the vial label. They can also be read instrumentally, using URITOP300 or MINI URITOP readers.

3. MATERIAL REQUIRED

- 1 vial with 100 strips with a color card on the vial.
- 1 instructions of use.

4. STORAGE AND STABILITY OF THE COMPONENTS

- Store the bottle closed at ambient or room temperatures between 2°C - 30°C (36°F - 86°F). Do not store the strips in a refrigerator or freezer.
- Store away from moisture and light.
- When stored in the original container, the product is stable up to the expiry date printed on the bottom of the container.
- **Note once the canister has been opened, the remaining strips remain stable for up to 6 months.** Beyond there is a risk of coloring or discoloration of the reagent pad further to an exposure in the humidity or in the light. Do not remove desiccant from the bottle.
- Replace the bottle cap immediately and tightly after removing test strips, and keep the vial tightly closed between tests.

5. PRECAUTIONS

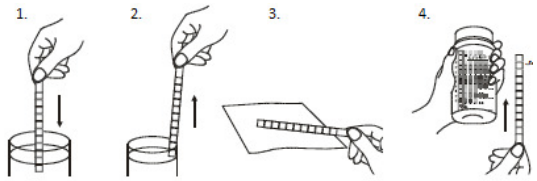
- For in vitro diagnostic use by professionals only.
- Do not touch test areas of urine reagent strips.
- Discoloration or darkening of the test pads may indicate deterioration. If this is evident, or if test results are questionable or inconsistent with expected finding, confirm that the product is within its expiration date and is reacting properly using known negative and positive control materials.
- Wear a smock, gloves and eye protection during the test. Avoid all contact with the skin and eyes.
- Do not eat, drink or smoke while handling the samples and while testing.
- The samples can be contaminated by infectious agents. Consider the material directly in contact with the samples as contaminated products. During the test, take the necessary precautions for the manipulation of infectious products.
- The test, when used, must be disposed of according to local procedures.

6. SAMPLE COLLECTION AND STORAGE

- Collect urine in a clean, dry container that allows complete immersion of all the fields on the test strip. Do not add preservatives. If cleanly voided specimens are not collected from females, positive results for leukocytes may be found due to contamination from outside the urinary tract.
- The use of fresh morning urine is recommended for optimal nitrite tests, as well as for the valid determination of bilirubin and urobilinogen, since these compounds are unstable when exposed to light.
- Test the sample within the hour following urination, with the sample well mixed but not centrifuged.
- If the test cannot be performed within one hour testing at room temperature, the sample should be stored in the refrigerator 2-8°C 4 hours, and then brought to room temperature before used in the test. Not frozen,
- Unpreserved urine at room temperature may undergo pH changes due to microbial proliferation, which may interfere with protein determination.
- Skin cleansers containing chlorhexidine may affect protein test results if specimen contamination occurs.

7. TEST PROCEDURE

The procedure must be followed exactly to achieve reliable results. Do not compare strips with color chart before the strip is dipped in urine.
a) Dip the strip into the urine up to the test area for no more than two second (see figure 1 below).
b) Draw the edge of the strip along the brim of the vessel to remove excess urine (see figure 2 below). At this time, don't make the test areas touched to the brim of the vessel.
c) Turn the strip on its side and tap once on a piece of absorbent material to remove any remaining urine (see figure 3 below). Excessive urine on the strip may cause the interaction of chemicals between adjacent reagent pads, so that an incorrect result may occur.
d) **For visually reading : Compare the colours of the reagent pads within 60 seconds (Leukocytes after 90~120 seconds)** with the color chart on the vial label under good light (see figure 4 below). While comparing, keep the strip horizontally to prevent possible mixing of chemicals when excessive urine is present.



For automatically reading using Uritop 300 or MINI URITOP reader : Carefully follow the directions given in the appropriate instrument operating manual. The instrument will automatically read each test pad result at a specified time.

8. RESULTS INTERPRETATION

Results are obtained by direct comparison of the printed color blocks on the color chard. The color blocks represent nominal values; actual values will vary so close to the nominal values.
In the event of unexpected or questionable results, the following steps are recommended: to confirm that the strips were tested before the expiration date printed on the bottle label or sealed bag, compare the results with positive and negative controls and repeat the test with a new strip. If the problem persists, do not use the test and contact the company Biosynex.

9. CHEMICAL PRINCIPLES OF PROCEDURE, INGREDIENTS AND LIMITATIONS

Blood:
Principle of procedure: The test is based on the Pseudo-peroxidase activity of the haem moiety of hemoglobin and myoglobin. The chromogen is oxidized by a hydroperoxide in the presence of haem and changes color from yellow (or greenish yellow) to blue.
Ingredients; Cumene Hydroperoxide 12mg, o-Tolidine 35mg.
Expected value: Normally, no hemoglobin is detectable in urine (0.010mg/dl; 3 RBC/µl). When hemoglobin appears in urine it indicates kidney disease or a urinary tract disorder. Blood may often be found in the urine of menstruating females.
The meaning of the presence of tracks of haemoglobin can vary according to the patients and the clinical situation. A clinical evaluation is necessary to estimate every particular case. The test is highly sensitive for the detection of the haemoglobin (it loses nevertheless in sensibility when erythrocytes are intact). It is a complement in the microscopic(tiny) examination.
Sensitivity : 10 erythrocytes/µL. The test is more sensitive in the presence of free haemoglobin or of myoglobine than in the presence of intact erythrocytes. The sensibility is decreased in the presence of urines with strong specific density or containing some ascorbic acid. The presence of green spots on the reactive zone indicates the presence of intact erythrocytes in the urine.
Limitation: Elevated specific gravity or protein in urine may reduce the reactivity of the blood test portion. Microbial peroxidase associated with urinary tract infection may cause false positive results. Ascorbic acid concentrations (>30 mg/dl) may cause false negatives at the low level of blood. It is important to re-suspend well red blood corpuscles before realizing the test. Do not use bowls of collection containing tracks of oxidizing substances (bleach for example). Take into account the risk of interferences bound in menstruation, the leucorrhoeas or a poll.

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Bilirubin:
Principle of procedure Azo-coupling reaction of bilirubin with a diazonium salt in an acid medium to form an azodye. Color changes from light tan to beige or light pink.
Ingredients: Sodium nitrite 0.733 mg, 2,4-dichlorobenzene diazonium 2.3mg, Sulfosalicylic acid 25mg.
Expected value: Normally no bilirubin is detectable in urine by even the most sensitive methods. Even trace amounts of bilirubin are sufficiently abnormal to require further investigation.
Sensitivity : 1 mg/dL
Limitation: Metabolites of drugs, such as pyridum and selenium, which give a color at low pH, may cause false positives. Indican (indoxyl sulfate) can produce a yellow-orange to red color response, which may interfere with the interpretation of negative or positive bilirubin readings. Ascorbic acid (> 30mg/dl) may cause false negative result. The search of bilirubin must be realized on an urin freshly emitted by avoiding the exposure prolonged in the light.

Urobilinogen:
Principle of procedure: The test is based on the Ehrlich's reaction. Color changes from light orange-pink to dark pink.
Ingredients: 4-Methoxybenzenediazonium 2.9mg
Epected values: The normal urobilinogen range is 0.1 to 1.0 Ehrlich unit /dl. If results exceed the concentration of 2.0 mg/dl, the patient and the urine specimen should be evaluated further.
Sensitivity: The test can detect concentrations of minimal urobilinogen of **0.1 mg/dL**. However, the absence of urobilinogen in the urine cannot be asserted. At the patients presenting a high rate of urobilinogen, the results are strictly correlated to the spectrophotométrie method of Watson-Schwartz.
Limitation: The absence of urobilinogen in the specimen cannot be determined. The test area will react with interfering substances known to react with Ehrlich's reagent, such as p-aminosalicylic acid. Drugs containing azo gantrisin may give a masking golden color. The test is not reliable method for the detection of porphobilinogen. The search of urobilinogen must be realized on an urin freshly emitted by avoiding the exposure prolonged in the light.

Ketones:
Principle of procedure : Legal's test-nitroprusside reaction. Acetoacetic acid in an alkaline medium reacts with nitroferricanide to produce a color change from beige to purple.
Ingredients: Sodium nitroprusside 23.0mg
Expected value: Ketone bodies should not be detected in normal urine specimens with this reagent.
Sensitivity: 5 – 15 mg/dL. Urine of fort specific density and of low pH can react. A clinical evaluation is thus necessary in presence draw of the ketones obtained with it reagent.
Limitation: Positive results (trace or less) may occur with highly pigmented urine specimens or those containing large amounts of levodopa metabolites. Some high SG and low pH urine may give false positive result. Phenosulfonphthalein may cause false positive result. A detectable rate of ketone bodies can seem in the urine during stress physiological such the jeun, the pregnancy, the physical exercise acido-cetose, the famine or in the presence of disorders of the glucidique or lipid metabolism. Ketone bodies can appear in the urine in great quantities before their rates rise in the serum. An important bactériurie can do a negative result.

Glucose:
Principle of procedure : Glucose oxidase catalyzes the oxidation of glucose to form hydrogen peroxide. The hydrogen peroxide thus formed then oxidizes a chromogen on the reaction pad by the action of peroxidase.
Ingredients: Glucose oxidase 430U, Peroxidase 200U, o-Tolidine 12mg
Expected value: A small amounts of glucose(up to 30mg/dl) are normally excreted by the kidney. The glucose is normally absent in some urine. It is nevertheless eliminated in small quantity by the kidney. A concentration of 50 mg / dL or more can be considered as abnormal especially if it is repeated.
Sensitivity: 50 – 100 mg of glucose / dL. The range of reading extends until 1000 mg / dL. The test is highly specific some glucose. The reactive zone does not react with the lactose, the galactose, the fructose or the reducing métabolites of salycilates and acid nalidixique.
Limitation : High SG (>1.020) with high pH urine and ascorbic acid (more than 40mg/dl) may cause false negative result at the low level of glucose. Do not use bowls of collection containing tracks of oxidizing substances (bleach for example).

Protein:
Principle of procedure : Protein "error of indicators." When pH is held constant by a buffer, indicator dyes release H^+ ions because of the protein present and change color from yellow (or greenish yellow) to blue-green.
Ingredients: Tetrabromophenol blue 0.34mg
Expected value: Normal urine specimens ordinarily contain some protein (<20mg/dL) therefore only persistent elevated levels of urine protein indicate kidney or urinary tract disease. The persistent results of trace level or over indicate significance proteinuria and thus further clinical testing is needed to evaluate the significant of results.
Sensitivity : 15 - 30 mg/dL of proteins.
Limitation: False positive results may be found in strongly basic urine (pH 9). The interpretation of results is also difficult in turbid urine specimens. Do not use bowls of collection containing tracks of oxidizing substances (bleach for example). Avoid toilet cleaned with salts of quaternary ammoniums (positive risk of forgery).

Nitrite:
Principle of procedure : The test is based on the diazotization reaction of nitrite with an aromatic amine to produce a diazonium salt. It is followed by an azo-coupling reaction of this diazonium salt with an aromatic compound on the reaction pad. The azo dye produced causes a color change form white to pink.
Ingredients: P-arsanilic acid 4.5mg
Expected value: Normally no nitrite is detectable in urine. Their presence indicates the presence of bacteria which can be responsible for renal infections, for the urethra, for the ureter or for the bladder.
Sensitivity: 0,05 mg/dL. The comparison of the coloring obtained against a white bottom can help in the detection of small quantities of nitrites which could not be detected otherwise. The test is specific nitrites and does not react with the other substances normally excreted in the urine.
Limitation: Ascorbic acid (>30mg/dL) may cause false negative result with low level of nitrite containing (<0.03mg) urine. The negative result does not always mean that the patient is free from bacteriuria. Pink spots or pink edges should not be interpreted as a positive result. Any pink uniform coloring indicates the presence of at least 105 bacteria / ml, but the intensity of the coloring is not proportional in the bactériurie. Negative result may occur when urinary tract infections are caused by organism which do not contain nitrate reductase; when urine has not been retained in the bladder long enough (four hours or more) for reduction of nitrate to nitrite occur; or when dietary nitrate is absent. An urine kept over a prolonged period can give false negative results and false positive results in case of bacterial contamination for example. The grip of nitres by-products can lead to false positive results.

Leukocyte:
Principle of procedure : This test pad contains an indoxyl ester and diazonium salt. It is followed by an azo-coupling reaction of the aromatic amine formed by leukocytes esterase with a diazonium salt on the reaction pad. The azo dye produced causes a color change from beige to violet**.**
Ingredients: Induced Indole amino acid ester 1.3mg
Expected value: Normally no leukocytes are detectable in urine**.**
Le résultat doit être interprété en fonction du contexte clinique notamment en présence de traces.
Sensitivity : The test can detect the presence of leukocytes to the state of track is **20~25 leukocytes/µℓ**.
Limitation: The test result may not always be consistent with the leukocyte cell number by the microscopic examination. High concentration of glucose, high specific gravity, high level of albumin, high concentration of formaldehyde or presence of blood may cause decreased test results. High concentration of oxalic acid of trace of oxidizing agents may cause false negative results.

pH:
Principle of procedure : Double indicator system. Indicator's methyl red and bromothymol blue are used to give distinct color changes from orange to green to blue. (**pH 5.0 to 9.0**)
Ingredients: Methyl red 0.05mg, Bromothymol blue 0.5mg
Expected value: Urine values generally range from pH 5 to 9. The urinary pH is an indicator importing certain metabolic situations bound to the functioning of the kidney and the systems gastroenteritis - intestinal and respiratory.
Sensitivity: Le test mesure des valeurs de pH situé entre **5 -9** avec une précision d'une unité.
Limitation: If the excessive urine is remain on the strip because of improper test procedure, it is possible that the acidic buffer in protein portion comes out and affect the pH portion, then pH result may be decreased than the actual. This phenomenon is called "run-over effect." The measure of the pH must be realized on an urine freshly emitted because a bacterial proliferation pulls an alcalinisation of the urine.

Specific Gravity (SG):
Principle of procedure : Ionic solutes present in the urine cause protons to be released from a polyelectrolyte. As the protons are released the pH decreases and produces a color change of bromothymol blue from blue-green to yellow-green.
Ingredients: Bromothymol blue 0.5mg, Poly (methyl vinyl ether/ maleique acid) anhydre 140.5mg.
Expected value : The normal SG of urine ranges from 1.001 to 1.035. The first morning urine possesses a specific density included between 1.015 and 1.025. The specific density of newborn children's urine varies 1.002 1.004. In case of severe renal hurts, the specific density is fixed to 1.010, value which corresponds to the density of the glomerulary filtrat.
Sensitivity: The test allows the determination of densities included between **1.000, 1.005, 1.010, 1.015, 1.020, 1.025**, **1.030**. stamped alkaline urines can give results by default.
Limitation: High-buffered alkaline urine may cause diminished result, whereas high-buffered acidic urine may cause slightly elevated result. A high specific density can be obtained in the presence of moderate quantities of proteins. The specific density also increases in the presence of glucose. A pH > 6.5 can pull a value by default of the specific density.

Ascorbic acid:
Principle of procedure : The test field involves the decolorization of Tillmann's reagent. The presence of ascorbic acid causes the color of the test field to change from gray-blue to yellow.
Ingredients: 2,6-dichloro indophenol sodium salt 0.8mg
Expected value : The average daily intake ranges from **30-80mg**, with an output of **20-30mg/day**.
Sensitivity : Low concentrations of ascorbic acid (until 50 mg / dL) in urines can cause interferences with samples containing of low concentration of glucose, blood and bilirubine. Concentrations equal or superior to 200 mg / dL can cause strong interferences. If we detect some ascorbic acid in the urine, to examine again after 24 hours without ingesting any ascorbic acid.

Limitation: No interferences are known.

Microalbumin:
Microalbuminuria, an abnormal elevation of the urinary albumin excretion rate, is often one of the first signs of renal disease or damage that can lead to renal failure. Patients with hypertension or diabetes have the highest risk of renal disease where microalbumin may be present. Microalbuminuria refers to small detectible amounts of albumin in the urine.
Principle of procedure: This test is based on dye binding using sulfonephthalein dye. At a constant pH, albumin binds with sulfonephthalein dye to develop a blue color. The resulting color ranges from pale green to aqua blue.
Ingredients: sulfonephthalein dye 0.1mg, Citric acid 30mg
Expected value: Normal albumin levels in urine are under 2mg/dl. Microalbuminuria is indicates with results of 3~30mg/dl.
Sensitivity: 3mg/dl (albumin)
Limitation: The following substances may cause false positive results: a large amount of hemoglobin(≥5mg/dl), visibly bloody urine, highly alkaline urine(pH>8), disinfectant including quaternary ammonium compound.

Creatinine:
Creatinine is a byproduct of muscle metabolism and creatinine excretion into the urine is usually constant. Creatinine measurement is used in the diagnosis and treatment of renal diseases, to monitor renal dialysis, and as a calculation basis for measuring other urine analytes. Though the concentration (or dilution) of urine varies throughout the day, the urinary creatinine level is relatively stable which allows its measurement to be used as a corrective factor in random/spot urine samples.
Principle of procedure: This test is based on the reaction of creatinine with a dye-metal complex. At an alkaline condition, creatinine reacts with a dye-metal complex to form a purplish-brown color complex.
Ingredients: picric acid 0.3mg, Borax 20mg
Expected value: The urine of healthy individuals contains 10~300mg/dl of creatinine. Very low creatinine results can be caused by adulteration of the urine specimen or by severe renal failure.
Limitation: Visibly dark brown color urine may affect the results. Substances that cause abnormal urine color, such as drug containing azo dyes, nitrofurantoin, riboflavin may affect the results.

Microalbumin to Creatinine Ratio:
When albumin and creatinine are measured simultaneously from a single-void / random urine sample, the albumin to creatinine ratio (ACR) can be determined. The ACR is the preferred test for screening of microalbuminuria recommended by the American Diabetes Association.

Principle of procedure: The following table is used to obtain the Microalbumin to creatinine ratio.

		Creatinine mg/dl(mmol/L)				
		10(0.9)	50(4.4)	100(8.8)	200(17.7)	300(26.5)
Microalbumin mg/dl(mg/L)	1(10)	*			Normal	
	3(30)					
	8(80)	High Abnormal		Abnormal		
	15(150)					

* Specimen is very dilute to decide accurately ratio result. Repeat test with new specimen, preferably a first-morning collection.

Examples:

Reading	Reported Result	Creatinine Result	Micoralbumin-to-Creatinne Ratio
Microalbumin=15mg/dL Protein=30mg/dL	30mg/dL	100mg/dL	Abnormal
Microalbumin=8mg/dL Protein=Negative	8mg/dL	300mg/dL	Normal

Microalbumin/Creatinine ratio Interpretation:

	Normal	Abnormal	High Abnormal
Conc. (mg/g)	<30	30-300	>300
Conc.(mg/mmol)	<3.4	3.4-33.9	>33.9

Expected value: Microalbumin is normally present in urine at concentrations of less than 30mg albumin / g creatinine. Microalbuminura is indicated at a ratio result of 30~300mg/g(Abnormal) and clinical albuminuria at a ratio result of >300mg/g(High Abnormal)
Limitation: A low microalbumin result (10mg/L) in combination with strongly diluted urine (creatinine result of 10mg/dl) could indicate a microalbumin concentration below the sensitivity limit. In the case, consider testing a new specimen, preferably a first morning collection, for greater confidence in the result.

10. QUALITY CONTROL
Controls are not supplied with this kit. The control is available under reference 6040001. It is recommended that controls are tested according to good laboratory practice to confirm the test procedure and to verify proper test performance on each new batch or each new delivery. Each lab should define its own quality control system.

11. PERFORMANCE AND CHARACTERISTICS
Performance characteristics are based on clinical and analytical studies and depend upon several factors: the variability of colour perception; the persence or absence of inhibitory and matrix factors typically found in urine; and the laboratory conditions in which the product is used (e.g., lighting, temperature,and humidity). Each colour block represents a range of values. Because of specimen and reading variability, specimens with analyte concentrations that fall between normal levels may give results at either level. Results will usually be within one level of the true concentration. The generally detectable levels of the analytes in contrived urines are indicated in section "expected value" of each parameters; however, because of the inherent variability of clinical urines, lesser concentrations may be detected under certain conditions.

12. BIBLIOGRAPHY
GP16-A: Urinalysis and Collection, Transportation, and Preservation of Urine Specimens; Approved Guideline (1992); National Committee for Clinical Laboratory and Approved Standards (NCCLS)

SYMBOLES / SYMBOLS

	Attention, Lire la notice d'utilisation Attention, see instructions for use	LOT	Numéro du lot Lot number
IVD	Pour diagnostic in vitro For *in vitro* diagnostic use only		Fabriquant Manufacturer
	A conserver entre 2-30°C Store between 2-30°C		Ne pas réutiliser Do not reuse
	Nombre de test par kit Tests per kit	REF	Référence catalogue Catalog number
	Date de péremption Expiry		

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