The early diagnosis of bladder cancer is important to successful local treatment. This study determined the clinical utility of NMP22 as a urinary marker for the early detection of transitional cell carcinoma (TCC) of the bladder in patients with hematuria or other indications at risk for malignancy. We also determined if NMP22 provided a cost advantage over our current modalities in our patient population. Each patient submitted a single voided urine which was divided in two parts, and tested for NMP22 and cytopathologic testing. All patients provided the urine samples before cystoscopic exam. Of the 330 patients, 114 (34.5%) presented with microscopic hematuria, and 66 (20.4%) with gross hematuria. Other indications for cystoscopy included atypical cytologies or unexplained voiding symptoms refractory to medical therapy. There were 18 patients with biopsy confirmed bladder cancer and 312 patients with benign conditions of the bladder. The median NMP22 value for the malignant bladder tumors (31.6 U/mL) was significantly higher than benign (4.3 U/mL) (P <0.001). The sensitivity of NMP22 was 100% with a specificity of 85% at a reference value of 10.0 U/mL, while cytology had a sensitivity of only 33% and a specificity of 100%. Given a negative predictive value of 100% for NMP22, a cost savings of $28,302 to $111,072 (depending on the type of insurance carrier) would have been achieved if it was used alone as the indication for cystoscopy. This study indicates that urinary NMP22 is a simple, non-invasive, cost-effective marker for the detection of bladder cancer.