Actas Urológicas Españolas. 2011;**35(2)**:65–71

Actas Urológicas Españolas

www.elsevier.es/actasuro

ORIGINAL ARTICLE

Cost-effectiveness of the combination therapy of dutasteride and tamsulosin in the treatment of benign prostatic hyperlasia in Spain

F. Antoñanzas[a], F. Brenes[b], J.M. Molero[c], A. Fernández-Pro[d], A. Huerta[e], R. Palencia[e], J.M. Cozar[f,*]

[a] *Departamento de Economía Aplicada, Universidad de la Rioja, Logroño, Spain*
[b] *Centro de Atención Primaria Llefià (ABS6), Badalona, Barcelona, Spain*
[c] *Centro de Salud San Andrés, Madrid, Spain*
[d] *Centro de Salud de Menasalbas, Toledo, Spain*
[e] *GlaxoSmithKline, Tres Cantos, Madrid, Spain*
[f] *Servicio de Urología, Hospital Universitario Virgen de las Nieves, Granada, Spain*

Received November 2, 2010; accepted November 5, 2010

KEYWORDS
Benign prostatic hyperplasia;
Combination therapy;
Dutasteride;
Tamsulosin;
Cost-effectiveness

Abstract
Objectives: To evaluate the incremental cost-effectiveness ratio (ICER) of the combination therapy with dutasteride and tamsulosin (DUT+TAM) as initiation treatment versus the most used drug in Spain, tamsulosin (TAM), in the treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH) with risk of progression.
Methods: A semi-Markov model was developed using 4-year and 35-year time horizons and from the Spanish National Healthcare Service perspective. Data was obtained from the CombAT trial. Effectiveness was measured in terms of quality adjusted life years (QALYs). An experts' panel defined healthcare resources and unitary costs were obtained from published Spanish sources. Pharmacologic cost is expressed in PTP_{WAT}; in the case of TAM, the generic price is used; in the case of DUT+TAM the price of a fixed-dose combination is used. Costs are expressed in 2010 Euros.
Results: Combination therapy with DUT+TAM produces an incremental effectiveness of 0.06QALY at year 4 and 0.4QALY at year 35. DUT+TAM represents an incremental cost of €810.53 at 4 years and €3,443.62 at 35 years. Therefore, the ICER for DUT+TAM versus TAM is €14,023.32/QALY at year 4 and €8,750.15/QALY at year 35.
Conclusions: Initiation treatment with DUT+TAM represents a cost-effective treatment versus TAM, the most used treatment in Spain, due to the fact the ICER is below the threshold that usually allows a technology to be considered as cost-effective.

*Corresponding author.
E-mail: cozarjm@yahoo.es (J.M. Cozar).

0210-4806/$ - see front matter

PALABRAS CLAVE
Hiperplasia benigna de próstata;
Combinación;
Tamsulosina;
Dutasterida;
Coste-efectividad

Coste-efectividad de la combinación dutasterida y tamsulosina en el tratamiento de la hiperplasia benigna de próstata en España

Resumen

Objetivos: Evaluar el coste-efectividad incremental (CEI) de la combinación dutasterida y tamsulosina (DUT + TAM) de inicio frente al tratamiento más utilizado, tamsulosina (TAM), en pacientes con hiperplasia benigna de próstata (HBP) moderada-grave con riesgo de progresión.

Material y métodos: Se diseñó un modelo semi-Markov con un horizonte temporal a 4 y a 35 años desde la perspectiva del Sistema Nacional de Salud español a partir del estudio CombAT. La efectividad de los tratamientos se midió en Años de Vida Ajustados por Calidad (AVAC). El uso de recursos sanitarios se obtuvo de un panel de expertos. Los costes unitarios proceden de tarifas publicadas por las Comunidades Autónomas. El coste del tratamiento farmacológico se expresa en PVP-IVA; en el caso de TAM se utilizó el precio del genérico y en el de DUT + TAM el de la combinación a dosis fija. Todos los costes se expresan en €2010.

Resultados: DUT + TAM produce una mejoría incremental respecto a TAM de 0,06 AVAC a los 4 años y de 0,4 AVAC a los 35 años. El coste incremental de DUT + TAM es de 810,53 € a los 4 años y 3.443,62 € a los 35 años. Por tanto, el CEI de TAM + DUT respecto a TAM es 14.023,32 €/ AVAC y 8.750,15 €/ AVAC a los 4 y 35 años respectivamente.

Conclusiones: El tratamiento de inicio con la combinación DUT + TAM es un tratamiento coste-efectivo frente TAM, el tratamiento más habitual en la práctica clínica española, al encontrarse el ratio CEI por debajo del umbral que usualmente se considera para clasificar las tecnologías como coste-efectivas.

Introduction

Benign prostate hyperplasia (BPH) is one of the most frequent pathologies in men. It is characterized by the chronic and progressive growth of the prostate gland, which causes the obstruction of urine outflow. It is clinically manifested in the so-called lower urinary tract symptoms (LUTS).[1] In more advanced stages, urine outflow obstruction may become chronic, where complications such as acute urinary retention (AUR), infection or kidney failure[2] arise. Likewise, patients may require surgery due to the disease itself or due to some of the complications.

There are currently two possible pharmacological alternatives for the treatment of BPH, the antagonists of alpha-adrenergic receptor (α-blockers), used to treat patient's LUTS, and the 5-alpha reductase inhibitors (5-ARI) that act on the progression of the disease. In Spain, the most used treatment is the tamsulosin uroselective alpha blocker.

The combination of a fixed-dose combination of tamsulosin and dutasteride 5-ARI has recently been marketed. The CombAT[3] study demonstrated that in patients with moderate to severe symptoms of BPH with the risk of progression, the combination is more efficacious in reducing the risk of AUR and/or surgery than monotherapy with tamsulosin.

At a health centre such as this one, where resources are limited, it is necessary to establish priorities for decision-making on the allocation of healthcare resources and the implementation of new technologies. This fact is especially important in the case of chronic and high-prevalence diseases such as BPH, which utilize a significant part of healthcare resources. Economic evaluation is a decision-making tool that is available to managers, as it allows assessing different healthcare interventions not only from the perspective of efficaciousness, but also based on effectiveness criteria. Within economic evaluation, one of the most used analyses is cost-effectiveness studies, which allow establishing a relation between the healthcare results obtained (e.g., hospitalizations avoided, life-years gained)[4] and the resources utilized (costs).

The aim of this study was to evaluate the cost-effectiveness ratio of initiating treatment with the combination therapy of dutasteride and tamsulosin versus tamsulosin monotherapy, the most used therapy in Spanish medicine, based on the results of the CombAT[3] study, from the perspective of the Spanish National Healthcare System.

Materials and methods

To be able to evaluate the differences in cost and effectiveness of initiating treatment with the combination of dutasteride and tamsulosin (DUT + TAM) versus tamsulosin (TAM) monotherapy, a semi-Markov economic model was designed based on the CombAT[3] study.

The model was designed following the methodological recommendations published,[5,6] with specification of the population included, the time horizon, the perspective and the discount rate, and a sensitivity analysis to verify the validity of the data was carried out.

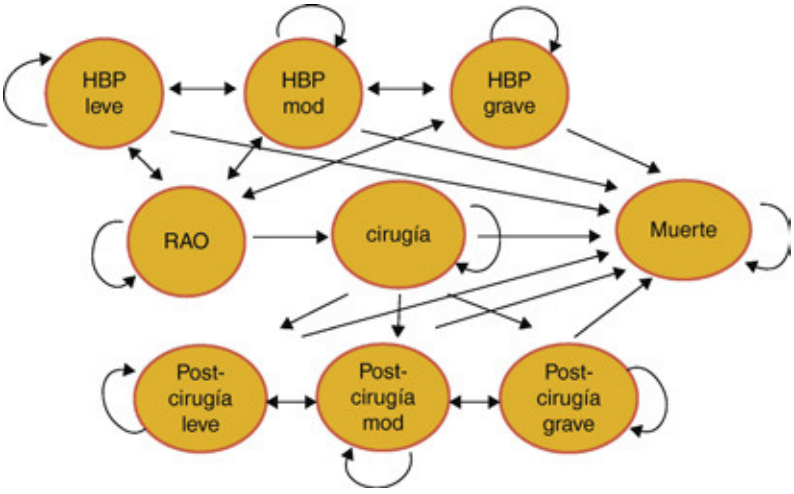

Figure 1 Graphic representation of the Markov model used in the study.

Description of the pharmacoeconomic model

The Markov model is a widely used pharmacoeconomic evaluation technique. In this type of model, the pathology studied is divided into a finite number of health states that patients experience in the course of discrete periods of time (Markov cycle), in accordance with a series of state-transition probabilities. By allocating an estimation of the use of healthcare resources to each of the health states and, subsequently, repeating this allocation throughout the time horizon of the model, it is possible to calculate the total costs that will be obtained in the patients included in the model.[7]

The model designed comprises nine health states that a patient may experience (fig. 1). The states were defined in accordance with the patient's clinical state (mild, moderate or severe symptoms of BPH,) and the complications he may suffer (AUR and/or surgery). Additionally, the absorbing death state to which the patients may evolve at any time of the model, whether due to BPH itself, to complications suffered or any other cause, was added. Each cycle lasted three months during the first four years, in accordance with the follow-up visits made during the CombAT[3] study and one year as of the fifth year of follow-up.

The model included men older than 60 years, with moderate to severe symptoms of BPH with the risk of progression (defined by prostate volume ≥30cm^3 and PSA: 1.5-10 ng/ml), in accordance with the population included in the CombAT[3] study. Patients were initially distributed based on the Miñana et al.[8] study, which studies patient distribution at Spanish urology surgeries in accordance with their clinical severity.

An initial time horizon of four years was used, which corresponds to the maximum follow-up time of the patients in the CombAT[3] study. As the treatment is chronic, and in accordance with the methodological recommendations of this type of studies,[5,6] a second analysis was carried out considering a time horizon of thirty-five years, which allowed adapting the model and lifelong treatment.[9] The perspective used was the Spanish National Healthcare System (SNS).

Transition probabilities

The transition probabilities between health states were obtained based on the clinical efficacy data of the TAM and DUT+TAM branches of treatment of the CombAT[3] study (table 1). After the fifth year, as no patient follow-up data was available, it was assumed that patients would evolve the same regardless of the treatment.[10]

Use of healthcare resources and related costs

The use of direct healthcare resources associated to each health state was obtained from a panel of three general practitioners and one urologist with ample experience in the treatment of BPH, authors of the consensus document "*Criterios de derivación en HBP para atención primaria*".[11] The unit costs of the healthcare resources are from the tariffs published by the Autonomous Regions. The cost of pharmacological treatment is expressed in RRP-VAT.[12] In the case of treatment with TAM, the price of generic drugs at the time the model was developed was used (Tamsulosin EFG); in the case of DUT + TAM, the price of the fixed-dose combination was used (Duodart®). Subsequently, and taking

Table 1 Probabilities of transition between health states, in accordance with results of the CombAT[3] study

	TAM	DUT+TAM
AUR RATE		
Annual rate/100 people	1.768	0.549
Annual cycle	0.018	0.005
3-month cycle	0.004	0.001
RATE of SURGERY		
Annual rate/100 people	2.036	0.613
Annual cycle	0.009	0.006
3-month cycle	0.002	0.001

AUR: acute urinary retention, TAM: tamsulosin, DUT: dutasteride.

Table 2 Quality-Adjusted Life Years (QALY) associated with each health state[16-19]

Health state	QALY
Asymptomatic person	1
Minor symptoms of BPH	0.99
Moderate symptoms of BPH	0.9
Severe symptoms of BPH	0.79
AUR	0.25
Surgery	0.25
Post-surgery state without symptoms	1
Post-surgery state - minor symptoms	0.99
Post-surgery state - moderate symptoms	0.89
Post-surgery state - severe symptoms	0.7
Death	0

into account that 68.7% of sales (units) of tamsulosin in Spain corresponds to modified release drugs[13] (Omic Ocas® and Urolosin Ocas®), a second analysis using the price of these drugs was carried out.

An annual discount rate of 3% was applied to correct the lower evaluation of the costs and the effectiveness results in the future.[6] All costs are expressed in 2010 euros.

Expression of results

The results of the model are shown as the incremental cost-effectiveness ratio (ICER) of the combination therapy DUT+TAM versus TAM, by means of the following formula:

$$\frac{Costes\ (DUT + TAM) - Costes\ (TAM)}{Efectividad\ (DUT + TAM) - Efectividad\ (TAM)}$$

The Quality-Adjusted Life Year (QALY) measurement of effectiveness was used. It is a measurement that indicates the relative preference of patients for a specific health state depending on life expectancy, morbidity or toxicity associated with a disease or treatment.[14] Thus, QALY can be considered as the numeric representation of the value of health in a single index that combines survival (life-years gained) and quality of life.[15] The QALY for the model was calculated based on studies in which the preferences associated with each health state[16-19] are defined (table 2).

Sensitivity analysis

Successive univariate sensitivity analyses were carried out with the parameters that were considered could undergo the most change in normal clinical practice, such as the clinical condition of patients, their age or level of healthcare where they are followed up, among others. The purpose of the sensitivity analysis was to minimize the impact of uncertainty in the results of the model.

Results

The use of healthcare resources associated with each health state, as well as the unit costs of each resource from the perspective the SNS are described in table 3. This data is from different Departments of Health and Healthcare Services and have been published in different Decrees, Laws and reports of institutions.

Table 3 Use of healthcare resources in patients with BPH and associated unit costs

Use of resources		Unit cost
TAM (Tamsulosin EFG)	Chronic treatment	€ 0,59/ day
DUT + TAM (Duodart®)	Chronic treatment	€ 1.30/ day
Visit to GP	3 visits first year	€ 26.27
	annual follow-up	€ 51.42
Visit to urologist	3 visits first year and 1 visit in case of worsening or annual follow-up	
Basic tests	Annual test	€ 25.13
PSA test	Annual test	€ 10.11
Urine sediment	Annual test	€ 2.53
Abdominal CT scan	Three-yearly test at GP	€ 65.23
Uroflowmetry	Three-yearly test at urologist	€ 178.02
AUR	60% non-emergency outpatients 40% emergency outpatients 2% admitted due to kidney failure removal of catheter additional visit to urologist	€ 238.86
SURGERY	65% transurethral resection 35% prostate adenectomy 80% no complications 20% complications follow-up visit to urologist After surgery patients: treatment with TAM	€ 2,808.33

The results of the cost-effectiveness model show how the initial treatment with DUT + TAM improves the health results of patients as a result of the proven reduction in the risk of suffering AUR or surgery.

Thus, treatment with DUT + TAM represents an incremental efficacy of 0.06 QALY with an incremental cost of € 810.53 at four years, versus TAM. At 35 years, treatment with DUT + TAM represents an incremental efficacy of 0.4 QALY, with an incremental cost of € 3,443.62.

The ICER of DUT + TAM with respect to TAM is € 14,023.32/ QALY at four years and € 8,750.15/ QALY at thirty-five years (table 4). The DUT + TAM ICER was calculated using the price of Omic Ocas®. In this case, the costs associated with TAM monotherapy treatment increased without effectiveness changing, which made the incremental costs of DUT + TAM with respect to TAM decrease to €364.70 at four years and to € 1,729.77 at thirty-five years, resulting in an ICER of € 6,310.57/ QALY at four years and € 4,397.94/ QALY at thirty-five years (table 5).

In Spain, although a unanimous criterion does not exist, it has been propounded that all treatments and surgical

Table 4 ICER Results setting 1 (tamsulosin EFG)

	QALY	Cost	Incremental effectiveness	Incremental cost	Cost/QALY
4 Years					
TAM	3.35	€ 1,373.90	0.06 QALY	€ 810.53	€ 14,023.32/QALY
DUT + TAM	3.41	€ 2,184.43			
35 Years					
TAM	13.28	€ 5,187.37	0.4 QALY	€ 3,443.62	€ 8,750.15/QALY
DUT + TAM	13.68	€ 8,630.99			

procedures with a cost lower than € 30,000/QALY could be considered to be cost-effective.[20] In accordance with the results of the model, which show an ICER below € 30,000/QALY, it can be considered that initiation with DUT + TAM fixed-dose combination therapy is a cost-effective treatment when compared to monotherapy with TAM.

Sensitivity analysis

Successive univariate sensitivity analyses were carried out modifying different parameters of the model to study whether the cost-effectiveness ratio changed. As shown in figure 2, initiation treatment with DUT + TAM continued to be a cost-effective treatment versus TAM (ICER <€ 30,000/QALY, as the parameters considered to have greater uncertainty in normal clinical practice changed.

Thus, for example, on modifying the population considered in the model to include only patients with severe symptoms of BPH, the ICER decreased to € 9,878.25/QALY at four years. If on the contrary, patient follow-up is modified and this is only done in urology, the follow-up costs increase and thus, the ICER also increases to € 15,295.86/QALY at four years, however, it is below the threshold of € 30,000/QALY.

It was also assessed if the cost-effectiveness ratio would change if the discount applied to costs and results were to be modified. Both on applying a greater discount (5%) and not applying any discount, DUT + TAM combination therapy continued to be a cost-effective treatment.

Discussion

Despite the growing importance of economic evaluation in informed decision-making, few studies have been published to date in Europe regarding the economic impact of the different therapeutic strategies for BPH, most of them mainly focused on the economic study of surgery.[16,21,22] In fact, this study is the first to be published in Spain that assesses the economic value for the SNS of a new drug with respect to the most used pharmacological treatment in clinical practice.

One of the critical points when developing a pharmacoeconomic model is its design, as it must accurately represent the disease studied. In this case, a Markov model was designed, as this model best allows representing the natural history of chronic diseases, simulating what occurs in the process of the disease[23] through the different health states.

In the model, a principal time horizon of four years was established, which corresponds to the maximum patient follow-up time in the CombAT[3] study. As BPH is a chronic disease whose complications increase in accordance with the patient's age, the aim was also to assess the result of a lifelong treatment (35 years) in line with the methodological recommendations published.[5,6] In this setting, the cost-effectiveness ratio decreased from € 14,023.32/QALY to € 8,750.15/QALY, indicating that the benefit of the DUT + TAM combination therapy is more evident in the long-term.

The population included in the model corresponds to the patients included in the CombAT[3] study, patients with moderate to severe symptoms of BPH and with the risk of progression; prostate volume ≥30cm^3, PSA: 1.5-10 ng/ml). In accordance with the Miñana et al.[8] study, this type of patients represents 64% of the patients that consult with urologists in Spain. The results of the economic model could not be extrapolated to the rest of the population with BPH as no data is available on the efficacy of the DUT + TAM combination therapy in other types of patients.

The results are expressed in the form of cost per QALY gained, as this measurement not only allows comparing

Table 5 ICER Results setting 2 (tamsulosin Ocas®)

	QALY	Cost	Incremental effectiveness	Incremental cost	Cost/QALY
4 Years					
TAM	3.35	€ 1,819.73	0.06 QALY	€ 364.70	€ 6,310.57/QALY
DUT + TAM	3.41	€ 2,184.43			
35 Years					
TAM	13.28	€ 6,901.22	0.4 QALY	€ 1,729.77	€ 4,397.94/QALY
DUT + TAM	13.68	€ 8,630.99			

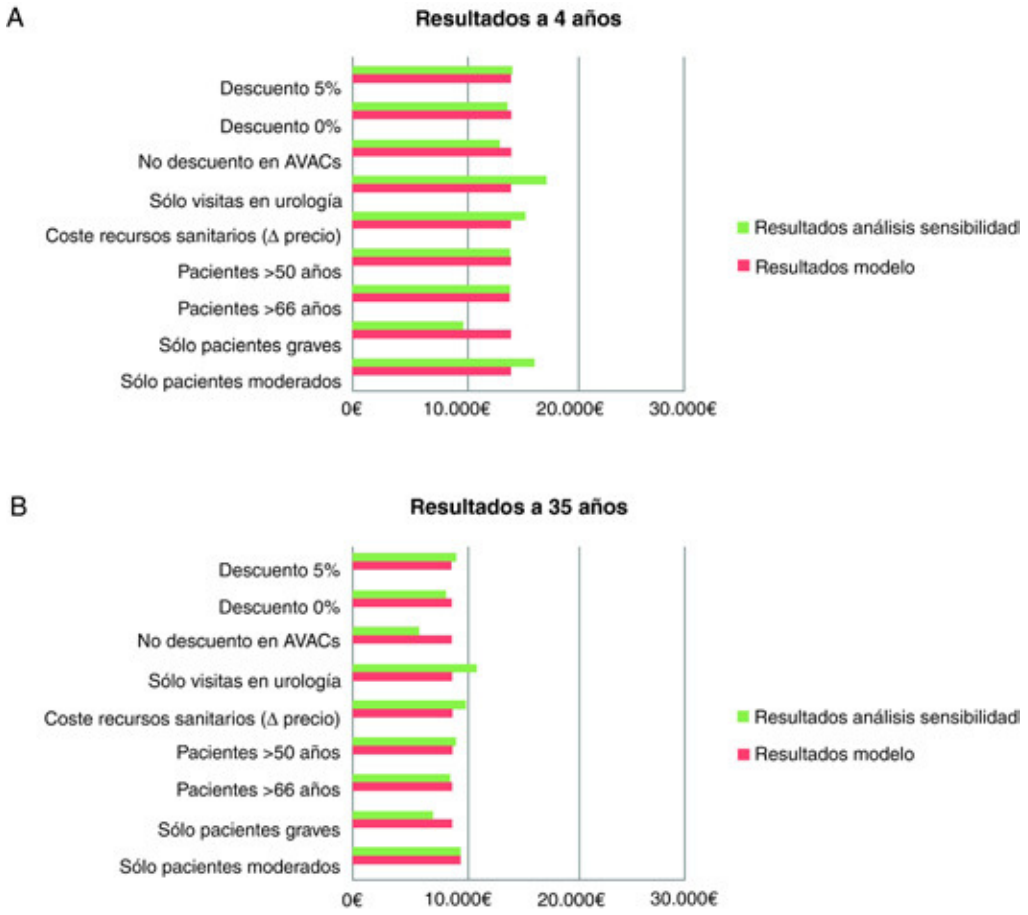

Figure 2 Results of the sensitivity analysis.

treatments for the same disease, but it also compares treatments aimed at different health problems. Taking into account the mean costs/QALY of other pathologies, we can conclude that DUT + TAM combination therapy would be an intervention with similar efficacy as breast cancer screening (€ 8,323/QALY)[4,24] or heart transplant (€ 11,290/QALY).[4,24] It is worth mentioning that the QALYs are a healthcare outcome measurement that is increasingly used by managers and decision-makers, as it allows making decisions regarding the distribution of healthcare resources among programmes or alternative interventions that compete with each other for those resources.

Likewise, the results of the economic evaluations, expressed in costs/QALY, are used routinely in the United States, Canada and many European countries in their drug funding processes. Thus, for example, in the United States and Canada, a healthcare intervention is considered to be cost-effective and therefore fundable if the cost/QALY is below 50,000 dollars.[25] In the case of Europe, the United Kingdom and other European countries, their threshold is set at £ 20,000-30,000/QALY.[26] As previously mentioned, in Spain, treatments whose cost is less than € 30,000 could be considered as cost-effective,[20] situating DUT+TAM combination therapy below the said threshold.

The principal results of the study were calculated using the price of TAM generics. However, according to IMS[13] market data, the tamsulosin most used in Spain is not the generic drug, but the modified release drug (Omic Ocas® y Urolosín Ocas®), which costs 56% more.[12] For this reason we carried out a second analysis using the price of Omic Ocas® to represent normal Spanish practice. In that case, the ICER of DUT + TAM decreased to € 4,379.94/QALY at thirty-five years, a value far from the threshold of € 30,000/QALY.

Ultimately, the results of the cost/effectiveness model show that initiation treatment with the fixed-dose dutasteride and tamsulosin combination therapy in patients with moderate to severe symptoms of BPH with the risk of progression is a cost-effective treatment versus monotherapy with tamsulosin, which is the normal treatment in clinical practice.[20] It would be recommendable to be able to follow-up patients under chronic treatment for the model with effectiveness data collected from clinical practice.

Funding

The study was funded by GlaxoSmithKline.

Conflict of interest

Doctors F. Antoñanzas, F. Brenes, J.M. Molero, A. Fernández-Pro and J.M. Cozar received frees from GlaxoSmithKline.

Doctors A Huerta and R Palencia are employees of GlaxoSmithKline.

References

1. Pérez N, Ortega NM, Brenes FJ. Hiperplasia benigna de próstata. Documentos clínicos SEMERGEN. Área Urología. 1st ed. Madrid: Edicomplet; 2008. p. 9-17.
2. O'Leary MP. Lower urinary tract symptoms/benign prostatic hyperplasia: Maintaining symptom control and reducing complications. Urology. 2003;62 Suppl 1:15-23.
3. Roehrborn CG, Siami P, Barkin J, Damião R, Major-Walker K, Nandi I, et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. Eur Urol. 2010;57:123-31.
4. Antoñanzas Villar FJ, Rubio-Terres C, Sacristán JA, Pinto JL, Prieto L, Rovira J. Análisis coste-efectividad en la evaluación económica de intervenciones sanitarias. Med Clin. 2004;122:505-10.
5. López Bastida J, Oliva J, Antoñanzas F, García-Altés A, Gisbert R, Mar J, et al. Propuesta de guía para la evaluación económica aplicada a las tecnologías sanitarias. Gac Sanit. 2010;24: 154-70.
6. Mar J, Antoñanzas F, Pradas R, Arrospide A. Los modelos de Markov probabilísticos en la evaluación económica de tecnologías sanitarias: una guía práctica. Gac Sanit. 2010;24: 209-14.
7. Rubio-Terres C, Echevarría A. Modelos de Markov: una herramienta útil para el análisis farmacoeconómico. Pharmacoec Sp Res Art. 2006;3:71-8.
8. Miñana B, Layola M, Prieto M. Distribución de Severidad Clínica y Prevalencia de Criterios de Progresión en Consulta de Urología en Pacientes con Hiperplasia Benigna de Próstata en España. LXXIV Congreso Nacional de Urología. 12-15 Junio 2009: Abstract C-41.
9. Datos de mortalidad de varones mayores de 60 años (2001). Available from: http://www.who.int/whosis/database/life tables/life table process.cfm?path=whosis,lifetables&language =english.
10. McConnell JD, Roehrborn CG, Bautista OM, Andriole Jr GL, Dixon CM, Kusek JW. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. NEJM. 2003;349: 2387-98.
11. Castiñeiras Fernández J, Cozar Olmo JM, Fernández-Pro A, Martín JA, Brenes Bermúdez FJ, Naval Pulido E, et al. Criterios de derivación en hiperplasia benigna de próstata para atención primaria. Actas Urol Esp. 2010;34:24-34.
12. Base de datos del Medicamento del Consejo General de Colegios Oficiales de Farmacéuticos. Catálogo de Especialidades Farmacéuticas. 2010. Available from: https://botplusweb.portalfarma.com/.
13. Base de datos IMS Health Dataview. Datos de ventas y prescripción en España. TAM. Agosto 2010.
14. Weinstein MC, Stason WB. Foundations of cost-effective analysis for health and medical practices. N Engl J Med. 1977; 296:716-21.
15. Froberg DG, Kane RL. Methodology for measuring healthstate preferences-II: scaling methods. J Clin Epidemiol. 1998;42:459-71.
16. Amin EA, Amin M. Comparison of the cost-effectiveness of various therapies for common prostatic disorders. Pharmacoeconomics. 1992;1:357-69.
17. Baladi JF, Menon D, Otten N. An economic evaluation of finasteride for treatment of benign prostatic hyperplasia. Pharmacoeconomics. 1996;9:443-54.
18. Flanigan RC, Reda DJ, Wasson JH, Anderson RJ, Abdellatif M, Bruskewitz RC. 5-year outcome of surgical resection and watchful waiting for men with moderately symptomatic benign prostatic hyperplasia: A department of veterans affairs cooperative study. J Urol. 1998;160:12-6.
19. Bissonni RS, Lawler FH, Holtgrave DR. Transurethral prostatectomay versus transurethral dilatiation of the prostatic urethra for benign prostatic hyperplasia: A cost-utility analysis. Famil Prac Res J. 1993;13:25-36.
20. Sacristán JA, Oliva J, del Llano J, Prieto L, Pinto JL. ¿Qué es una tecnología sanitaria eficiente en España? Gac Sanit. 2002; 16:334-43.
21. Ahlstrand C, Carlsson P, Jonsson B. An estimate of the life-time costs of surgical treatment of patients with benign prostatic hyperplasia In Sweeden. Scan J Urol Nephro. 1996;30:37-43.
22. Lowe FC, McDaniel RC, Chmiel JJ, Hillman AL. Economic modeling to assess the costs of treatment with finsateride, terazosin, transurectal resection of the prostate for men with moderate to severe symptoms of benign prostatic hyperplasia. Urology. 1995;46:477-83.
23. Briggs A, Sculpher M. An introduction to Markov modeling for economic evaluation. Pharmacoeconomics. 1998;13:397-409.
24. López y Casanovas G, Ortún Rubio V. Economía de la salud, fundamentos y políticas. Madrid: Ediciones Encuentro; 1998.
25. Gafni A, Birch S. Guidelines for the adoption of new technologies: a prescription for uncontroleed growth in expenditures and how to avoid the problem. CAMJ. 1993;148: 913-7.
26. McCabe C, Claxton K, Culyer AJ. The NICE Cost-Effectiveness Threshold. What it is and what it means. Pharmacoeconomics. 2008;26:733-44.