# COMPARISONS OF COSTS RELATED TO THE INITIATION OF TAPENTADOL OR OXYCODONE TREATMENT IN SPANISH PATIENTS SUFFERING FROM CHRONIC SEVERE NON-MALIGNANT PAIN

PSY15

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## Introduction

- Tapentadol is an atypical opioid that acts as a µ-opioid receptor agonist and noradrenaline reuptake inhibitor, with both mechanisms contributing to its analgesic effect [13]
- It provides similar pain relief compared to oxycodone, whereas its gastrointestinal tolerability is significantly improved, thereby resulting in fewer treatment discontinuations compared to oxycodone [1]
- In a previous cost-effectiveness analysis for the treatment of non-malignant pain in Spain tapentadol dominated oxycodone, showing better quality of life outcomes at lower costs [2]
- In the meantime a new co-payment scheme was issued in Spain and numerous newly launched generics relevantly reduced oxycodone drug costs
- The aim of this study was not only to update the cost-comparison, but also to focus on the first month, which commonly represents a dose titration period when analgesia and side effects are evaluated and the appropriateness of therapy for the individual patient is assessed

## Methods

- An analytic model was built with the following health states:
  - adequate pain management with no adverse events (AEs) and no treatment discontinuation
  - AEs but no discontinuation
  - discontinuation due to AEs
  - discontinuation due to lack of efficacy
- In case of discontinuation it was assumed that the patients will receive alternative opioid therapy for pain relief
- Probabilities of events (AEs, discontinuations) were derived from 3 RCTs with defined in- and exclusion criteria as reported previously [2] (Figure 1). The 2 populations are comparable regarding age, gender, pain severity, comorbidities, and prior opioid experience at baseline.
- Health care resource utilization and unit cost data were derived from published sources and official price list, thereby accounting for the following Spanish particularities
  - a new co-payment scheme, issued in 2012, considering a reimbursement rate based on declared income and labor (retired/non-retired)
  - a 7.5% price reduction for drugs not included in the reference price system, according to Royal Decree Law 08/2010
- All costs were estimated for year 2018
- An overview of the calculated average reimbursement rate, valid for patients treated with strong opioids, as well as all costs considered in the model are summarized in Table 1

**Table 1** Reimbursement rate and costs considered in the analytic model

| Parameter | Value | References |
|---|---|---|
| Reimbursement rate | 61.13% | Considering a proportion of patients on strong opioids being retired [2], the distribution of income in retired and non-retired population [3], and the reimbursement rates valid for the defined income ranges [4] in Spain (rate calculated for 27% >65y, 73% non-retired) [2] |
| Daily tapentadol costs | 3.07 € | Calculated for an average titration dosage of 240 mg [2], considering Spanish price list [5] |
| Daily oxycodone costs | 1.09 € | Calculated for an average titration dosage of 40 mg [2], considering Spanish price list [5] |
| Daily alternative opioid costs | 2.24 € | Calculated as average daily drug price of morphine, transdermal fentanyl, transdermal buprenorphine and oxycodone/naloxone, considering average doses [2],[6] and Spanish price list [5] |
| Daily additional opioid costs | 2.60 € | Applies to all opioid treatments and includes costs for 2 GP visits [7], as well as costs for laxatives [2],[5], thereby assuming that 40% of Spanish patients treated with strong opioids receive preventive laxatives [8] |
| Constipation event costs | 111.52 € | Average value from 3 sources [2],[8],[9], inflation adjusted to 2018 according to the National Statistics Institute (Instituto Nacional de Estadistica) |
| Switching costs | 147.12 € | Additional physician's consultation costs associated with the switch, considering the mean number of physicians visits per switch [2], the average number of switches to achieve adequate pain relief [10], and the cost of specialists visits [7] |
| Indirect costs | | Number of days off were calculated from a Swedish study [11], which already accounted for an employment rate of 23.4% in patients treated with strong opioids. Costs per day from absenteeism were derived from Spanish study [12], inflation adjusted according to the National Statistics Institute (Instituto Nacional de Estadistica) |
| – Patients with no AEs, no discontinuation | 173.20 € | |
| – Patients with AEs, no discontinuation | 207.78 € | |
| – Patients with AEs leading to discontinuation | 260.67 € | |
| – Patients with discontinuation due to lack of efficacy | 260.67 € | |

- Total costs were calculated for the first month from the perspective of the Spanish National Health System (NHS), considering the reimbursed proportion of direct costs, as well as from societal perspective, also including co-payment and indirect costs

**The following general aspects should be considered in the context of the products specific labeling**

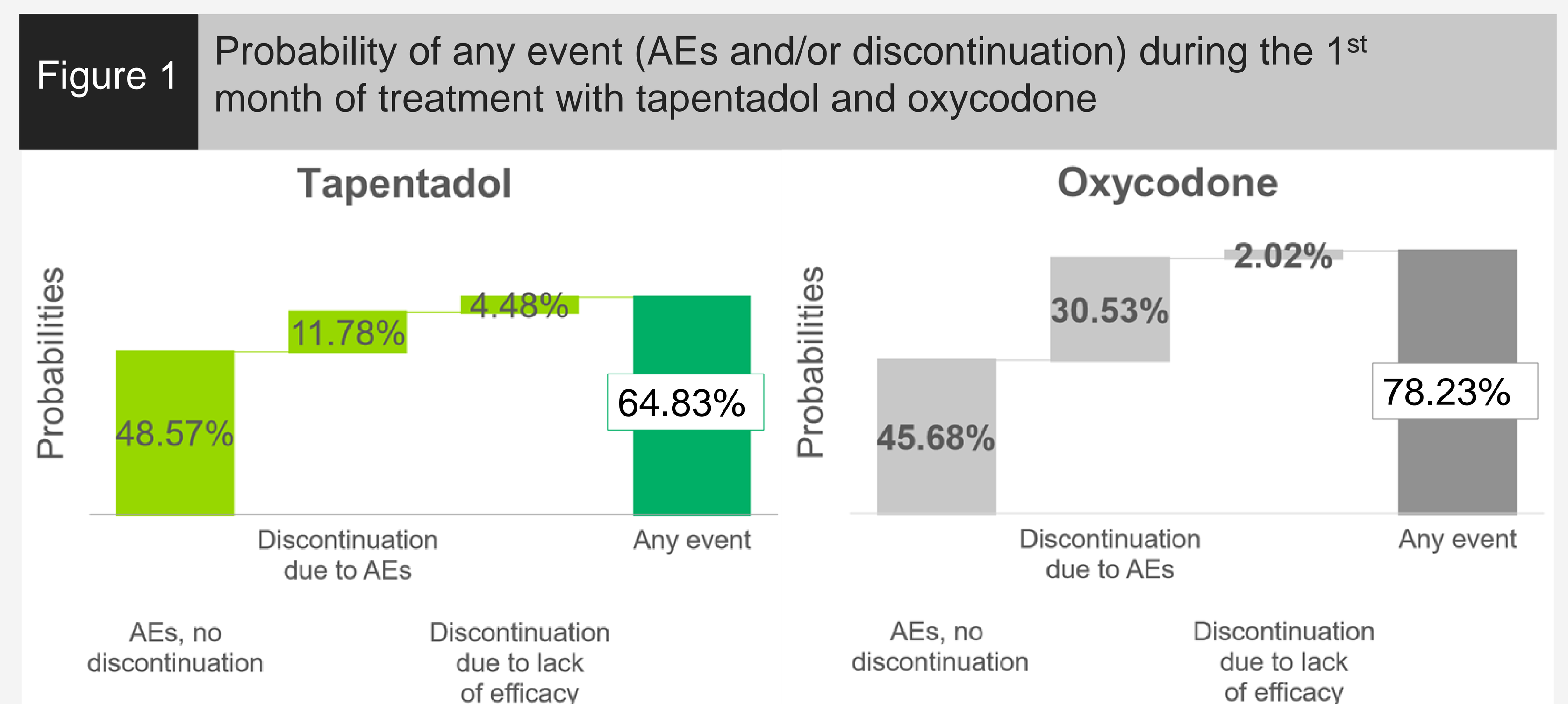
- Individualise, patient-centered approach for diagnosis and treatment of pain is essential to establish a therapeutic alliance between patient and clinician. Consider patient variables that may affect opioid-dose in patients prior to opioid therapy (1)
- Patients should be carefully selected and regularly monitored to ensure that opioids are prescribed appropriately (3-4)
- Clear treatment goals related to pain and function should be agreed with the patient (3-4)
- Patients should be made aware of the potential opioid side effects and the potential of tolerance, dependence and addiction (3-4)
- Addiction is possible even when opioids are taken as directed. The exact prevalence of addiction in patients treated with opioids for chronic pain is difficult to determine.(5)
- Regular clinical reviews are required for long-term opioid therapy, to assess pain control, impact on lifestyle, physical and psychological well-being, side effects and continued need for treatment(2), e.g.
  - Patients should be monitored throughout opioid treatment to reassess the benefits and risks of continued therapy. If benefits do not outweigh risks, reconsider the treatment plans and if doses of opioids should be tapered down or discontinued. (3-4)
  - When opioids are used long-term, patients should be kept under close surveillance (2)
  - Signs of addictive behavior should be monitored and addressed. (3-4)
- Patients and the general public can benefit from clear educational materials and awareness interventions to enhance their opioid related literacy and reduce stigma (6)

1. FDA Pain Management Best Practices May 2019 2. O'Brien T et al. Eur J Pain 2017;21:3-192
3. Faculty of Pain Medicine, Opioids Aware https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware Accessed September 2019 4. Kosten TR et al, Scie Pract. Perspect 2002;1:13-20 5. Rosenblum A et al Exp. Clin. Psychopharmacol. 2008;16(5):405-416 6. OECD Health Policy. Addressing Problematic opioid use in OECD Countries May 2019 http://www.oecd.org/health/addressing-problematic-opioid-use-in-oecd-countries-a18286f0-en.htm

## Results

- The risk of AEs not leading to discontinuation was only slightly higher with tapentadol, whereas the risk of discontinuation (withdrawal due to AEs and due to lack of efficacy) from oxycodone treatment was nearly double the risk of tapentadol (32.6% for oxycodone versus 16.3% for tapentadol)
- Accordingly the risk of any event (AEs and/or discontinuation) during the first month was increased by 20% with oxycodone
- Probabilities are graphically displayed in Figure 1

**Figure 1** Probability of any event (AEs and/or discontinuation) during the 1st month of treatment with tapentadol and oxycodone




- Considering the costs associated with AEs and opioid switches, higher daily treatment costs with tapentadol were totally offset, leading to cost savings with tapentadol during the first month of treatment
  - from the perspective of the Spanish NHS, total costs were calculated at 226.05 € for tapentadol versus 237.22 € for oxycodone (Figure 2)
  - from societal perspective total costs were calculated at 465.78 € for tapentadol versus 470.80 € for oxycodone (Figure 3)

**Figure 2** Total costs for the 1st month of treatment with tapentadol and oxycodone from the perspective of the NHS

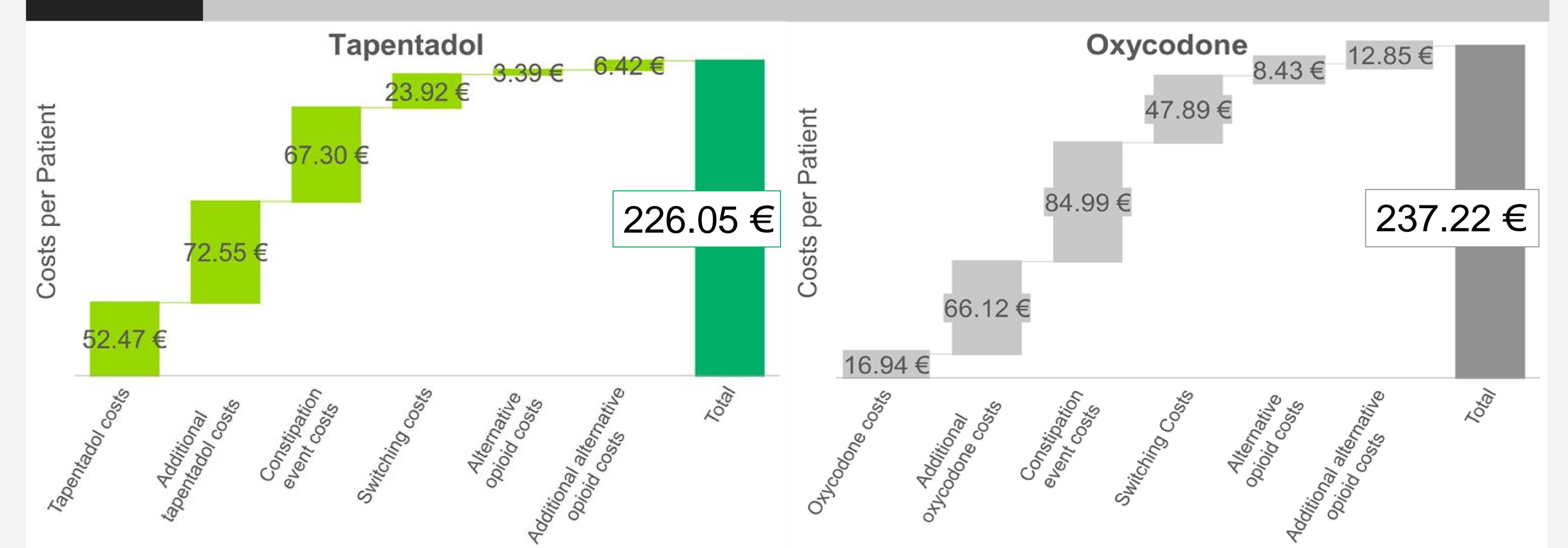
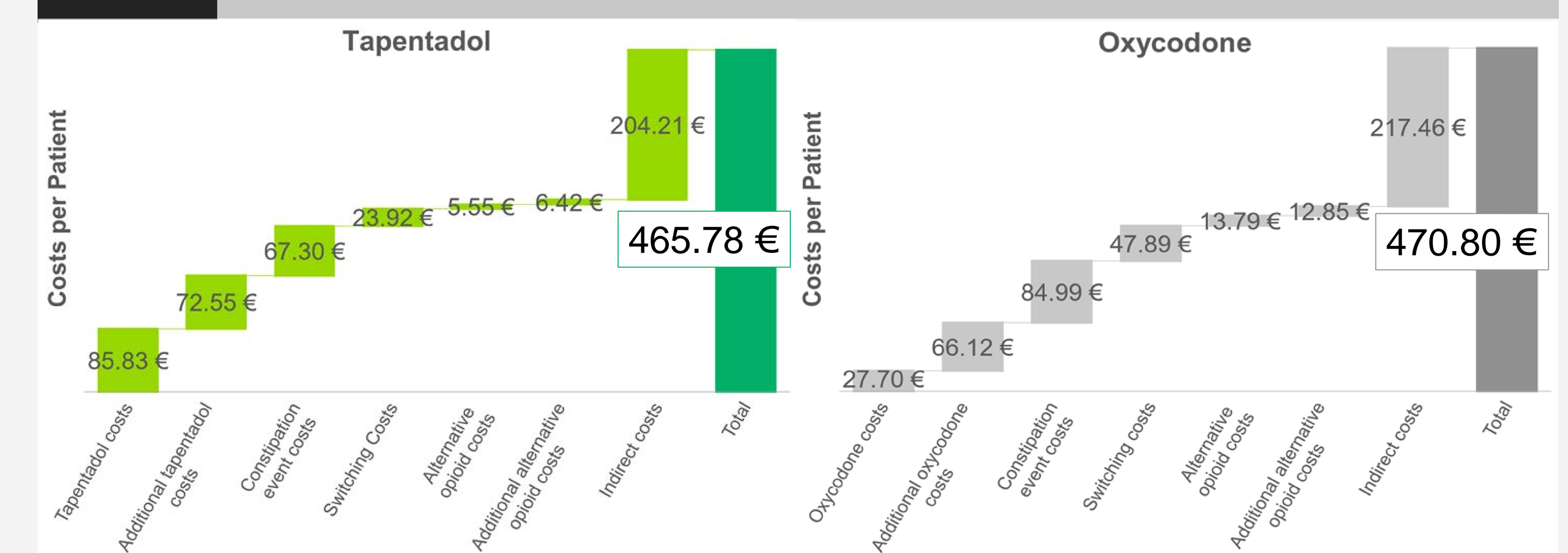



**Figure 3** Total costs for the 1st month of treatment with tapentadol and oxycodone from societal perspective




## Conclusions

- Despite higher drug costs compared to generic oxycodone, tapentadol's better tolerability and the associated lower risk of treatment discontinuation results in cost-savings during the first month of treatment of non-malignant pain in Spain
- Accordingly, the physician can individually assess the appropriateness of tapentadol treatment for patients with chronic severe LBP without increasing total costs for the NHS or society during this titration/assessment phase

## References:

[1] Lange et al. Adv Ther 2010; 27:381-399. [2] Obradovic et al. Clin Ther 2012; 34:926-943. [3] Saborido & Sánchez 2014; available from http://www.rtihs.org/sites/default/files/25450%20 Saborido_ISPOR._Poster.pdf. [4] Ministry of Health, available from: www.msssi.gob.es. [5] Spanish Vademecum 2018; available from https://www.vademecum.es/. [6] Ikenberg et al. J Med Econ 2012; 15:724-736. [7] Gisbert & Brosa (Update 2018); available from http://www.oblikue.com/bddcostes/. [8] Gálvez et al. Pharmacoeconomics Span Res Art 2012; 9:23-34. [9] Guijarro et al. Value Health 2010; 13:A369. [10] Gonzales-Barboteo et al. J Opioid Manag 2014; 10:395-403. [11] Hjalte et al. J Pain Symptom Manage 2010; 40:696-703. [12] Mainar et al. Clinicoecon Outcomes Res 2012; 4:39-47. [13] Tzschentke et al. Drugs Today 2009, 45:483-496.

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