Modeling the Frequency and Costs Associated with Postsurgical Gastrointestinal Adverse Events for Tapentadol IR versus Oxycodone IR

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Background: Few studies have estimated the economic effect of using an opioid that is associated with lower rates of gastrointestinal (GI) adverse events (AEs) than another opioid for postsurgical pain.

Objective: To estimate the number of postsurgical GI events and incremental hospital costs, including potential savings, associated with lower GI AE rates, for tapentadol immediate release (IR) versus oxycodone IR, using a literature-based calculator.

Methods: An electronic spreadsheet–based cost calculator was developed to estimate the total number of GI AEs (ie, nausea, vomiting, or constipation) and incremental costs to a hospital when using tapentadol IR 100 mg versus oxycodone IR 15 mg, in a hypothetical cohort of 1500 hospitalized patients requiring short-acting opioids for postsurgical pain. Data inputs were chosen from recently published, well-designed studies, including GI AE rates from a previously published phase 3 clinical trial of postsurgical patients who received these 2 opioids; GI event–related incremental length of stay from a large US hospital database; drug costs using wholesale acquisition costs in 2011 US dollars; and average hospitalization cost from the 2009 Healthcare Cost and Utilization Project database. The base case assumed that 5% (chosen as a conservative estimate) of patients admitted to the hospital would shift from oxycodone IR to tapentadol IR.

Results: In this hypothetical cohort of 1500 hospitalized patients, replacing 5% of oxycodone IR 15-mg use with tapentadol IR 100-mg use predicted reductions in the total number of GI events from 1095 to 1085, and in the total cost of GI AEs from $2,978,400 to $2,949,840. This cost reduction translates to a net savings of $22,922 after factoring in drug cost. For individual GI events, the net savings were $26,491 for nausea; $12,212 for vomiting; and $7187 for constipation.

Conclusion: Using tapentadol IR in place of a traditional μ-opioid shows the potential for reduced GI events and subsequent cost-savings in the postsurgical hospital setting. In the absence of sufficient real-world data, this literature-based cost calculator may assist hospital Pharmacy & Therapeutics committees in their evaluation of the costs of opioid-related GI events.

Pain is a global health problem that affects 1 of 5 adults in the community and occurs in 43% to 77% of the approximate 35.1 million patients who are hospitalized annually in the United States. Pain is ubiquitous among the nearly 30.2 million people who undergo inpatient surgery annually in the United States. Opioid analgesics are a mainstay of postsurgical pain management, but are often associated with treatment-limiting gastrointestinal (GI), central nervous system, and respiratory adverse events (AEs). Of these, opioid-related GI AEs are the most common, with an incidence rate of 10% to 32% for nausea and/or vomiting and 15% to 41% for constipation. These GI AEs are particularly troublesome after surgery, because they can...
Tapentadol is a centrally acting analgesic with 2 mechanisms of action—μ-opioid receptor agonism and norepinephrine reuptake inhibition, which may help to minimize GI events.

Previous studies have shown that tapentadol IR causes fewer GI events than oxycodone IR in the postsurgical setting.

This new study compared the total GI events and associated incremental costs for tapentadol IR versus oxycodone IR in the postsurgical setting from a hospital perspective, using a cost calculator and a hypothetical cohort of 1500 hospitalized patients requiring short-acting opioids.

Replacing 5% of oxycodone IR 15-mg use with tapentadol IR 100 mg reduced the total number of postsurgical GI events from 1095 to 1085, which was associated with a cost reduction from $2,978,400 to $2,949,840.

Individual GI event net savings for the 5% use of tapentadol IR instead of oxycodone IR were $26,491 for nausea, $12,212 for vomiting, and $7187 for constipation.

The potential cost-savings associated with reduced GI events seen with tapentadol IR versus oxycodone IR in the postsurgical setting may suggest the need to look beyond drug-acquisition cost to consider the effect on net costs of care when making formulary decisions.

Key Points

- Opioid analgesics, a key to postsurgical pain management, are associated with lower gastrointestinal (GI) and other adverse event rates.
- Unlike traditional opioids, such as oxycodone IR, that exert analgesic activity by binding to μ-opioid receptors, tapentadol IR has a second mechanism involving norepinephrine reuptake inhibition, which may help to minimize GI events.
- Previous studies have shown that tapentadol IR causes fewer GI events than oxycodone IR in the postsurgical setting.
- This new study compared the total GI events and associated incremental costs for tapentadol IR versus oxycodone IR in the postsurgical setting from a hospital perspective, using a cost calculator and a hypothetical cohort of 1500 hospitalized patients requiring short-acting opioids.
- Replacing 5% of oxycodone IR 15-mg use with tapentadol IR 100 mg reduced the total number of postsurgical GI events from 1095 to 1085, which was associated with a cost reduction from $2,978,400 to $2,949,840.
- Individual GI event net savings for the 5% use of tapentadol IR instead of oxycodone IR were $26,491 for nausea, $12,212 for vomiting, and $7187 for constipation.
- The potential cost-savings associated with reduced GI events seen with tapentadol IR versus oxycodone IR in the postsurgical setting may suggest the need to look beyond drug-acquisition cost to consider the effect on net costs of care when making formulary decisions.

Exacerbate anesthesia-induced nausea and decreased GI motility, sometimes resulting in ileus. Furthermore, GI AEs are associated with increased healthcare resource utilization because of additional medications used to manage the GI AEs and an increase in hospital length of stay (LOS).7,10,13-17

The guidelines for managing surgery-related pain advocate a multimodal, opioid-sparing approach to improve analgesic activity and to minimize the risk for opioid-related AEs.6,18 Most traditional opioids exert analgesic activity by binding to μ-opioid receptors in the brain; these receptors are also present in the GI tract. Tapentadol is a centrally acting analgesic with 2 mechanisms of action—μ-opioid receptor agonism and norepinephrine reuptake inhibition.19,20 These 2 mechanisms of action may account for the significant analgesia, along with the lower incidence and intensity of AEs that are normally associated with traditional μ-opioid receptor agonists, such as oxycodone.21

In 2 phase 3 studies of patients with acute pain, including postoperative pain, the incidence of GI AEs was lower with tapentadol immediate release (IR) than with oxycodone IR at equianalgesic doses, including dose strengths other than tapentadol IR 100 mg.2,23

We chose oxycodone IR as the traditional opioid because of its inclusion in guidelines for surgery-related pain,6 the availability of pivotal clinical studies comparing oxycodone IR with tapentadol IR,21,24 and its spectrum of AEs that is similar to that of tapentadol IR,23,24

Although the clinical benefits of using opioids with different mechanisms of action are well documented, few studies have examined the potential economic effect of this strategy in postsurgical populations.

The objective of this study was to estimate the number of potential reductions in postsurgical GI AEs and incremental hospital costs for GI event rates associated with tapentadol IR versus oxycodone IR, using a literature-based calculator. The analysis focused on data related to postsurgical GI AE rates, because of their availability in the published literature.

Methods

Study Design

We developed a cost calculator using literature-based data to estimate the number of postsurgical GI AEs and the costs associated with incremental hospital LOS for tapentadol IR versus oxycodone IR. Studies were chosen on the basis of their recent publication date, the relevance of AE end points evaluated in the study, the clinical setting, and the quality of the study design.

The model estimated the GI AEs for a hypothetical cohort of 1500 hospitalized patients using Schedule II short-acting opioids for the management of moderate-to-severe acute postsurgical pain.

The model assumed that tapentadol IR 100 mg could be substituted for oxycodone IR 15 mg (each given every 4 to 6 hours), because of the availability of published trial results suggesting that these dosages were equianalgesic for postsurgical pain.24 The GI AEs were considered collectively and individually, and included composite GI AEs (ie, nausea, vomiting, and/or constipation); nausea and/or vomiting; nausea; vomiting; and constipation.

Data Sources for GI AE Rates and Length of Stay

We obtained the GI AE rates from 2 randomized, double-blind, multicenter phase 3 trials conducted by Johnson & Johnson Pharmaceutical Research & Development between 2006 and 2007 (Table 1).24,25 For the base-case analysis, we used data from a trial of 603 pa-
patients with moderate-to-severe acute postsurgical pain evaluated over 72 hours who were randomized to receive tapentadol IR, oxycodone IR, or placebo.24

For the base-case analysis, LOS data for patients who experienced AEs were obtained from a retrospective cohort study of an inpatient database of 450 hospitals used in the study by Suh and colleagues (Table 1).15 In this study, the total treatment costs and hospital LOS were compared for 2 cohorts who received analgesics—patients who received medications for nausea, vomiting, and/or constipation and patients who did not. The use of medication for nausea, vomiting, and/or constipation was a proxy for a nausea, vomiting, and/or constipation event. The proxy, however, was defined to minimize the risk of including prophylactic use by excluding patients who received nausea, vomiting, and/or constipation medications during the 6-month period before the initiation of analgesics; patients who received a medication for nausea, vomiting, and/or constipation on the first day of treatment with analgesics did not. The use of medication for nausea, vomiting, and/or constipation was a proxy for a nausea, vomiting, and/or constipation event. The proxy, however, was defined to minimize the risk of including prophylactic use by excluding patients who received nausea, vomiting, and/or constipation medications during the 6-month period before the initiation of analgesics; patients who received a medication for nausea, vomiting, and/or constipation on the first day of treatment with analgesics were also excluded.15 A generalized linear model with log link function and gamma distribution was used to estimate the LOS for the 2 cohorts, adjusting for potential confounders (eg, type of analgesics received, age, sex, comorbidities, surgical procedures, number of prescription drugs received during hospital stay). More than 50% of the patients receiving analgesics subsequently received medications for the management of GI AEs, which are associated with longer hospital LOS and higher treatment costs.15

To simulate the target population for our model, we focused on patients who received oral analgesics rather than the overall population of patients who received injectable and/or oral analgesics, including nonopioids. The hospital LOS for the base case was the difference between the predicted, covariate-adjusted LOS with and without GI medication (Table 1).

For the sensitivity analysis, we applied GI AE rates from an outpatient 90-day trial of 878 patients with moderate-to-severe lower back pain or osteoarthritis of the hip or knee for ≥3 months who were randomized to receive tapentadol IR or oxycodone IR.25 The hospital LOS data from a retrospective chart and an electronic medical records review of a random sample of 402 patients who underwent orthopedic surgery were used for an additional sensitivity analysis.26 In this study, the effect of opioid-related AEs, including GI AEs, on the hospital LOS was examined. Bivariate and multivariate analyses were performed to identify potential predictors of postsurgical LOS. Vomiting and constipation were associated with longer postsurgical LOS after adjusting for other variables.26

<table>
<thead>
<tr>
<th>Table 1</th>
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<td>Cost per day of hospital stay, $</td>
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*a Gastrointestinal AEs as a system organ class may include AEs beyond nausea, vomiting, and constipation.

*b Incremental LOS was calculated as the difference between LOS for nausea/vomiting/constipation (6.48 – 5.12 = 1.36) or nausea/vomiting (6.31 – 5.12 = 1.19), and no nausea/vomiting/constipation (5.12), which was used as the reference value.

*c Wholesale acquisition cost per tablet ($3.23) multiplied by number of daily doses (5.06) and mean LOS (4.6 days).27

AE indicates adverse event; HCUP, Healthcare Cost and Utilization Project; IR, immediate release; LOS, length of stay; NR, not reported.
**Figure 1** Estimated Total Number of GI\(^a\) AEs and Related Costs, Before and After Use of Tapentadol IR

\(^{a}\text{GI refers to composite GI events, including nausea, vomiting, and/or constipation.}\)

AE indicates adverse event; GI, gastrointestinal; IR, immediate release.

### Calculator Structure and Analysis

Three types of calculations were performed using the spreadsheet model. These calculations were repeated under the assumption of no tapentadol use, followed by a shift to tapentadol. First, we calculated the number of GI AEs as the cohort size multiplied by the rate of AEs of interest. Second, we calculated the cost of GI AEs as the number of GI AEs multiplied by the incremental hospital LOS (in days) resulting from GI AEs, multiplied by the daily cost of the hospital stay. Third, we calculated the net costs as the cost of GI AEs minus the incremental cost of using tapentadol IR instead of oxycodone IR. Mathematical calculations were performed using Excel 2007 (Microsoft Corporation; Redmond, WA).

The model required several inputs, including cohort size; GI AE rates for tapentadol IR and oxycodone IR\(^{24,25}\); incremental hospital LOS resulting from GI AEs\(^{15}\); percent allocation of the oxycodone IR and tapentadol IR treatments; tapentadol IR cost\(^{27}\) using wholesale acquisition cost in 2011 US dollars; and daily cost of hospital stay (Table 1).\(^{28}\)

The cohort size was chosen arbitrarily. The cost of oxycodone IR was excluded (ie, conservatively set at $0.00) because of the availability of inexpensive generic formulations. All other treatment costs (eg, nursing time, drug treatments) were assumed to be reflected in the LOS cost, because it was based on average hospitalization costs.

In the base-case analysis, tapentadol IR was assumed to represent 5% of the use of short-acting opioids to control acute postsurgical pain in the hypothetical hospital setting; the use of oxycodone IR was set at 95%. Two separate data points were used for the hospital LOS—incremental LOS of patients who used nausea, vomiting, and/or constipation medication versus patients who did not, and incremental LOS of patients who used nausea and/or vomiting medication versus patients who did not use nausea, vomiting, and/or constipation medication.\(^{15}\) Because both data points reflected differences in LOS compared with patients who did not use nausea, vomiting, and/or constipation medication, no adjustment was made.

We performed several sensitivity analyses (Table 1). In the first sensitivity analysis, the shift rate for tapentadol IR was changed from 5% to 10% and 2%. In the second analysis, the cohort size was changed from 1500 patients to 1000 and 2000 patients. Third, the hospital LOS was varied by ±25%. Fourth, the cost of tapentadol IR was varied by ±25%. Fifth, we applied a different set of GI AE rates using data from a randomized trial of patients with lower back pain or osteoarthritis.\(^{25}\) In this 90-day safety trial, the AE rates for tapentadol IR versus oxycodone IR were 44.2% versus 63.5% for GI, and 18.4% versus 29.4% for nausea.\(^{25}\) Finally, we explored the impact of increasing incremental LOS while adjusting the cost of tapentadol IR per hospital stay, using data from the chart review study.\(^{26}\) Relative to the base-case analysis, the LOS was increased by 7%, 15%, and 40%, and the cost of tapentadol IR was adjusted using a mean LOS of 3.2 days (vs 4.6 days in the base-case analysis\(^{15}\)), resulting in a drug cost of $52.30 per hospital stay.

### Results

In the base-case analysis of composite GI AEs in the 1500-patient hypothetical cohort, replacing 5% of oxycodone IR 15-mg use with tapentadol IR 100 mg was associated with decreases in the number of GI AEs, from 1095 to 1085, and in the overall cost, from $2,978,400 to $2,949,840 (Figure 1). The cost was reduced by $28,560, resulting in a net savings of $22,922 after factoring in drug cost, or approximately $2300 per event avoided. For nausea and/or vomiting, replacing 5% of oxycodone IR 15 mg was associated with a decrease in the number of nausea and/or vomiting AEs from 1050 to 1037, and a total cost reduction from $2,499,000 to $2,468,655. The cost was reduced by $30,345, resulting in a net savings of $24,707 after factoring in drug cost.

In the base-case analysis of individual GI AEs, replacing 5% of oxycodone IR 15-mg use with tapentadol IR 100 mg was associated with findings similar to those for the composite GI AEs. For nausea, the cost was reduced by $32,130, resulting in a net savings of $26,491 after factoring in drug cost. The corresponding cost reductions...
and net savings after factoring in drug cost were $17,850 and $12,212, respectively, for vomiting and $12,825 and $7187, respectively, for constipation.

In the sensitivity analyses, replacing 10% of oxycodone IR 15-mg use with tapentadol IR 100 mg was associated with a net savings of $45,843, whereas replacing 2% use was associated with a net savings of $9169 (Figure 2).

Increasing the cohort size to 2000 patients was associated with a net savings of $30,562, whereas decreasing the size to 1000 patients was associated with a net savings of $15,281. The effects of varying the incremental hospital LOS and drug cost are shown in Figure 2; the effect of varying the GI AE rate is shown in Table 2. Increasing the incremental hospital LOS by 7% was associated with a net savings of $26,637, whereas increasing the LOS by 40% was associated with a net savings of $36,061 (Table 2).

A final sensitivity analysis was conducted to establish the worst-case and break-even scenarios for the LOS. For the worst-case scenario, the assumption was made that the incremental LOS for the composite GI AEs was zero days when replacing 5% of oxycodone in the base-case analysis with tapentadol IR while using the other parameters from the base case. The result yielded a net cost increase of $5639, which accounts for the difference in the acquisition cost of tapentadol IR 100 mg. The break-even analysis was done to determine the minimum incremental LOS for the composite GI AEs required for the base-case analysis (5%) to yield a cost-neutral result. An incremental LOS of a little more than 25% of 1 day (ie, 0.27 days) yielded a neutral net cost. These analyses demonstrated the relatively small change necessary to achieve cost benefits with tapentadol IR.

**Discussion**

Our analyses demonstrate the potential cost-savings associated with replacing oxycodone IR with tapentadol IR in hospitalized patients who are experiencing acute postsurgical pain under the assumption (based on published data) that treatment-related GI AEs result in a longer hospital LOS. The difference in the acquisition cost of tapentadol IR 100 mg compared with that of oxycodone IR 15 mg (set at $0.00) was offset by the savings associated with a reduction in the incidence of GI AEs, resulting in a net savings of $22,922, or approximately $2300 per event avoided. These savings are likely as a result of improving patient health status.

As recommended by the Panel on Cost-Effectiveness in Health and Medicine, we varied the model inputs to provide estimates for alternative scenarios. For example, we considered the GI AE rates from a 90-day randomized, double-blind safety trial. This was done to simulate clinical practice in an outpatient setting, because the GI AE rate may differ from that in the hospital. In
the safety trial, nausea was reported in 29.4% of patients who received oxycodone IR, which is within the range reported for patients receiving opioid analgesics in systematic reviews and in a large cohort study of hospitalized patients.

We performed sensitivity testing to assess the uncertainty of the model’s inputs. Over the ranges tested, the cost-calculator model was the most sensitive to the change in the percentage of tapentadol IR use (ie, shift rate; Figure 2). The model provides linear estimates for net costs based on market share: a market share that is twice as large will yield a cost-savings that is twice as large. Comparing selected model inputs with worst-case and break-even scenarios provides a perspective on the size of the change needed to result in an overall cost-savings. As long as there is a modest increase in the hospital LOS (ie, 0.27 days) that is associated with GI AEs, the model will predict savings. The model was least sensitive to the acquisition cost of tapentadol IR.

The model used data from published studies for inputs, such as the hospital LOS for the base-case analysis. Specifically, we chose a retrospective cohort study of the Premier Perspective database, the largest inpatient drug utilization database in the United States. We also used a published study that was based on patients undergoing orthopedic surgery, and examined the effect of opioid-related AEs (including GI AEs) on inpatient LOS using medical records from 2007, to provide a relevant perspective on the size of the change needed to result in an overall cost-savings. As long as there is a modest increase in the hospital LOS (ie, 0.27 days) that is associated with GI AEs, the model will predict savings. The model was least sensitive to the acquisition cost of tapentadol IR.

Our model focused on GI AEs because they are most frequently associated with opioids, particularly bothersome in postsurgical patients, and can interfere with pain relief. Specifically, in the clinical trial used for our model inputs, tapentadol IR 100 mg was associated with lower incidences of GI AEs versus oxycodone IR 15 mg, including nausea (49% vs 67%, respectively), vomiting (32% vs 42%), and constipation (10% vs 15%).

In the second study used in our model, the use of tapentadol IR 50 mg or 100 mg versus oxycodone IR was associated with lower incidences of any GI AE (44.2% vs 63.5%, respectively), nausea (18.4% vs 29.4%, respectively; P < .001), vomiting (16.9% vs 30.0%, respectively; P < .001), and constipation (12.8% vs 27.1%, respectively; P < .001), but not diarrhea (6.6% vs 5.9%, respectively) and dry mouth (5.3% vs 2.9%, respectively).

In addition, studies documenting the economic burden associated with GI AEs are available, which allowed us to develop the economic calculator for this study. The cost-saving drivers were primarily from event avoidance (ie, decreased hospital LOS), with some savings offset by a higher cost for tapentadol IR. In other words, the costs of AEs are incremental inpatient LOS. We assumed no additional costs for medications used to treat these AEs, and simply multiplied the average cost of a daily hospital stay by the percentage LOS increase to estimate the cost of an AE.

The estimated decreased LOS for the avoidance of AEs is modeled on the rate of AEs from the 2 clinical trials mentioned earlier, as well as for a database study that assessed the impact of AEs on LOS, in which patients who were not receiving a medication for nausea, vomiting, and/or constipation had a 1.36-day decreased LOS. The model assumed a hospital cost of $2000 daily, using the Healthcare Cost and Utilization Project (HCUP) 2009 national estimate. After incorporating higher drug cost, the model estimated a net savings of approximately $2300 for a GI event avoided.

The approximate $2300 net savings per nausea, vomiting, and/or constipation event avoided as predicted by the cost calculator was similar to the savings reported in one study, but was higher than in 2 other studies, which may be a result of the differences in methods, timing, or study population. Our drug costs were calculated in 2011 US dollars, and hospital costs were based on 2009 costs.

Similar to our findings, Suh and colleagues estimated that the additional cost associated with the treatment of nausea, vomiting, and/or constipation in hospitalized patients who received opioid analgesics was $2223; data for this retrospective cohort study were collected between 2005 and 2007.

By contrast, Kwong and colleagues estimated that inpatient service costs within 3 months after the initiation of an index opioid prescription in the outpatient setting were approximately $1900 higher for patients with prescription claims for antinaemics or laxatives than for patients with no GI events or therapies; data for this retrospective database study with multivariate regression analysis were collected between 2002 and 2005.

Oderda and colleagues estimated that the additional cost associated with opioid-related AEs—including GI and non-GI AEs—was $840 in surgical patients at a university hospital; data for this retrospective matched cohort study were collected in the 1990s.

Our findings have clinical and economic implications. From a clinical perspective, the burden of acute pain comprises inadequate analgesia and treatment-related GI AEs; although cause and effect have not been demonstrated, the evidence suggests that these 2 components are related. In a recent survey of more than 50,000 patients with moderate-to-severe acute pain, including postsurgical pain, 44% of patients received potentially inadequate analgesia and 28% had at least 1 GI AE. Patients who received inadequate analgesia were more likely to take their opioid medication in smaller
doses or less frequently because of GI AEs than patients who received adequate analgesia.9

Inadequate treatment of postsurgical pain can lead to needless suffering, impairment of health-related quality of life, readmission for further pain treatment, and the development of chronic pain.10 Of note, fewer recipients of tapentadol IR stopped treatment because of any AEs than recipients of oxycodone IR in the 90-day safety trial.25

From a hospital perspective, the economic burden of acute pain comprises direct costs associated with drug acquisition, pharmacologic interventions, extended LOS, and intangible costs (ie, burden on hospital personnel resulting from the time required to relieve pain and to manage treatment-related AEs, as well as the emotional toll of caring for patients suffering from inadequate pain relief).

Collectively, these findings suggest that the use of an opioid with a dual mechanism of action and an improved tolerability profile may offer an attractive alternative for managing the clinical and economic burden of postsurgical pain. This may be of relevance to hospital Pharmacy & Therapeutics (P&T) committees, especially when the Centers for Medicare & Medicaid Services implements value-based purchasing and considers patient response (eg, pain-management domain) on the Hospital Consumer Assessment of Healthcare Providers and Systems Survey as a determinant of hospital reimbursement and performance.

Limitations

Our study has several limitations that may affect its generalizability. The cost calculator was designed to estimate potentially lower costs associated with replacing oxycodone IR with tapentadol IR, as long as the rate of GI AEs associated with tapentadol IR was lower. Clinical trials comparing the 2 analgesics consistently demonstrated lower nausea, vomiting, and/or constipation rates for the patients receiving tapentadol IR than for patients receiving oxycodone IR.22-25 Therefore, the model estimates only lower potential event costs, because the number of nausea, vomiting, and/or constipation events for switching to tapentadol IR would be lower.

In addition, the calculator did not include other oral opioid agents, because comparative data were not available.

Our analysis included data from a previously published clinical trial,24 a study using an administrative claims database,15 and national hospital discharge data.28 Clinical trials provide input parameters that demonstrate outcomes under ideal clinical circumstances (ie, efficacy), and may not reflect real-world utilization and outcomes (ie, effectiveness). Although the use of an administrative claims database provides for a generalizable insured population, and the study design allows for the inclusion of a more diverse patient population compared with patients studied within the confines of clinical trials, residual methodologic bias and coding or documentation errors are possible. Confounders were adjusted in the administrative claims-based study, and the results revealed the potential effect on LOS while patients were using opioids.

The hypothetical cohort of 1500 surgeries requiring postoperative opioid therapy was chosen arbitrarily, given the marked variability among hospitals in the number of surgeries performed depending on the patient–physician mix. Therefore, we performed sensitivity analysis with cohorts of 1000 and 2000 surgeries to demonstrate the effect of varying this input. We might have underestimated the overall cost, because HCUP had only made available its 2009 costs in US dollars at the time of this project.

These findings suggest that the use of an opioid with a dual mechanism of action and an improved tolerability profile may offer an attractive alternative for managing the clinical and economic burden of postsurgical pain.

We did not include AEs involving the central nervous system, respiratory system, or other non-GI systems. The overall rate of any AE was similar for tapentadol IR 100 mg and oxycodone IR 15 mg (85% vs 87%, respectively) in one of the model input studies,24 suggesting the potential for different outcomes if all AEs had been considered. P values were not provided for these comparisons but are included below whenever available.

In a post hoc analysis, tapentadol IR was associated with less nausea or vomiting (53% vs 70%, respectively; P = .007) and numerically lower incidences of headache (12% vs 14%, respectively), generalized pruritus (7% vs 10%, respectively), hyperhidrosis (4% vs 6%, respectively), and pyrexia (0% vs 2%, respectively) versus oxycodone IR 15 mg.24 The only AEs with numerically higher incidences for tapentadol IR versus for oxycodone IR 15 mg were dizziness (31% vs 30%, respectively), somnolence (21% vs 10%, respectively), and pruritus (17% vs 12%, respectively).24 In the second model input study, the non-GI AEs associated with tapentadol IR 50 mg or 100 mg versus oxycodone IR were dizziness (18.1% vs 17.1%, respectively; P > .05), headache (11.5% vs 10.0%, respectively), somnolence (10.2% vs 9.4%, respectively; P > .05), fatigue (5.6% vs 2.4%, respectively), and pruritus (4.3% vs 11.8%, respectively).25 Therefore, the lack of significant differences in non-GI AEs supports our decision to model GI AEs only.
Conclusions

The results of this cost calculator using previously published data demonstrate the potential GI GI-related cost-savings for a hospital by using tapentadol IR in place of a traditional μ-opioid. Studies are needed to determine the clinical value of these findings and to validate their economic implications in the real-world setting. In the absence of sufficient real-world data, a literature-based modeling approach using a cost calculator may assist hospital P&T committees to assess the cost impact of opioid-related GI AEs on their inpatient populations. This study reaffirms the need to look beyond drug acquisition cost and to consider the effect on net costs of care when making formulary decisions related to opioid use in the postsurgical inpatient setting.

Acknowledgments

The authors would like to thank Cindy W. Hamilton, PharmD, ELS, of Hamilton House (Virginia Beach, VA) for assisting with manuscript preparation. Hamilton House received compensation from Janssen Scientific Affairs, LLC, for its contributions.

Funding Source

This study, including manuscript preparation, was supported by funding from Janssen Scientific Affairs, LLC (formerly Ortho-McNeil Janssen Scientific Affairs, LLC).

Author Disclosure Statement

Mr Paris and Dr Kozma received research funding and writing support from Janssen Scientific Affairs, LLC; Dr Chow is an employee and stockholder of Janssen Scientific Affairs, LLC; Ms Patel was formerly a contractor for Janssen Scientific Affairs, LLC; Dr Mody is an employee of Janssen Scientific Affairs, LLC, and a shareholder of Johnson & Johnson; Dr Kim is an employee of Johnson & Johnson and a stockholder of Janssen Scientific Affairs, LLC.

References

STAKEHOLDER PERSPECTIVE

Can Substituting Generic Drugs with Brand-Name Agents for Acute Pain Postsurgery Help to Deliver Cost-Effective, Quality Care?

By Matthew Mitchell, PharmD, MBA
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Payers/Hospitals: The use of brand-name drugs in the place of generic therapeutic alternatives always gets the attention of payers. Justifying the replacement of a generic, standard-of-care medication requires the demonstration of better efficacy, safety, and/or superior cost-effectiveness. Paris and colleagues created a model to demonstrate potential cost offsets with a hypothetical replacement of a portion of oxycodone immediate release (IR) with tapentadol IR in a postsurgical setting. A lower incidence of gastrointestinal (GI) adverse events was extrapolated from an active comparator study with oxycodone after bunionectomy. Cost-savings resulting from a lower rate of GI adverse events in the outpatient setting are difficult to ascertain, particularly if a visit to an urgent care facility or an emergency department is not required. Outside of the possible use of antiemetics, of which several inexpensive generics are available, the majority of intervention-based costs are for over-the-counter medications used for constipation, as well as agents for adequate hydration. The majority of other expenditures are indirect costs. The model created by the authors suggests a substantial cost-savings when replacing oxycodone IR with tapentadol IR for use after surgery in the hospital setting. The majority of the cost-savings, according to this model, results from a lower required hospital length of stay if oxycodone IR is replaced by tapentadol IR. The cost of tapentadol IR was modeled at $52.30 daily compared with no cost for oxycodone; however, this is inconsequential, because of the increased length of stay by almost 2 days for the group using oxycodone IR compared with the group using tapentadol IR.

Many health plans cover hospital stays based on a diagnosis-related group payment. Hospitals may be incentivized to deliver the most efficient care possible, including eliminating extended stays resulting from medication-induced adverse events.

These data may generate interest in evaluating real-world data with the use of observational analyses. If the data are in line with these published cost-savings, hospitals may be wise to evaluate standing orders for acute pain control and determine if, or when, a substitution, such as tapentadol IR, should be used.

In implementing accountable care models of risk and reimbursement, these types of analyses will become even more important for delivering cost-effective, quality care.

Patients: A lower rate of GI adverse events has been shown with tapentadol IR compared with oxycodone IR, which can clearly be beneficial for patients undergoing surgery, in addition to the reduced number of days at the hospital. If these numbers are borne out by real-world data, the advantage of switching from a generic medication to a brand-name drug in the context of postsurgical acute pain may become evident for patients as well.