The safety profile of parecoxib for the treatment of postoperative pain: an examination of over 10 years of postauthorization safety data

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INTRODUCTION

- Traditional nonselective nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 specific inhibitors (COXIBs) have the potential to elicit a variety of adverse events (AEs).¹⁻⁴
- The risk for some events, such as gastrointestinal (GI)-related ulceration events and perioperative bleeding, is reduced with the use of COXIBs compared with NSAIDs.^{1,5,6}
- Parecoxib, an injectable COXIB and prodrug of valdecoxib, is approved in >80 countries as perioperative analgesia to reduce postoperative pain and, in some of these countries, to treat acute pain.
- Parecoxib first received regulatory approval in 2001. Thus, there is a wealth of postauthorization safety data available.
- This study utilized postauthorization safety data to examine the occurrence of predefined safety events, commonly associated with traditional NSAIDs and/or COXIBs, in patients treated with parecoxib for the management of postoperative pain.

METHODS

- Data were derived from a Pfizer database, which captures all reported AE information from across the world.
 - AEs are coded to a specific Medical Dictionary for Regulatory Activities (MedDRA) term within the database.
- The database was searched for specific MedDRA terms or standard MedDRA queries corresponding to predefined safety events (see **Table**).
- The number of medically confirmed cases, along with outcome, through March 31, 2014 was presented for each event.
 - Individual cases were categorized as medically confirmed based on guidelines from the European Medical Agency guidelines on good pharmacovigilance practices (module VI) and the International Conference on Harmonization (E2B).

RESULTS

- It is estimated that 69,567,300 units of parecoxib were sold from the first quarter of 2002 through the first quarter of 2014.
- The total number of reports/number of reports classified as serious for each event over this period was as follows (**Table 1**):
 - GI ulceration-related events (n=35/35)
 - Renal failure and impairment (n=77/68)
 - Cardiovascular embolic and thrombotic events (n=66/64)
 - Hypersensitivity reactions (n=190/98), including severe hypotension (n=32/25) and severe cutaneous AEs (n=17/17)
 - Masking signs of inflammation (n=18/18).
- Among reports with known outcomes, a majority of patients recovered or were recovering from these events (**Table**).
- A total of 46 fatalities, which cannot be confirmed as treatment-related, were reported (**Table**):
 - Cardiovascular embolic and thrombotic events (n=20)
 - Renal failure and impairment (n=6)
 - GI ulceration-related events (n=4)
 - Hypersensitivity reactions (n=7), including severe hypotension (n=3) and severe cutaneous AEs (n=2)
 - Masking signs of inflammation (n=4).

LIMITATIONS

- It is difficult to definitively attribute these events and their outcomes, including fatalities, to parecoxib for the following reasons:
 - Although physicians report AEs they deem related to parecoxib treatment, there is no placebo for direct comparison.
 - Patients often receive other medications, in addition to parecoxib, that may contribute to the event in question.
 - Key information may be missing from the database, including age and dose and/or duration of treatment.

Table. Occurrence of important safety risks among parecoxib-treated patients

Pre-defined event	Total, n	Serious, n	Outcome
GI ulceration-related event	35	35	Recovered = 12 Recovering = 3 Not recovered = 4 Unknown = 12 Fatal = 4
Renal failure and impairment	77	68	Recovered = 32 Recovering = 9 Recovering with sequela = 1 Not recovered = 8 Unknown = 21 Fatal = 6
Cardiovascular embolic and thrombotic event	66	64	Recovered = 20 Recovering = 4 Recovering with sequela = 2 Not recovered = 2 Unknown = 18 Fatal = 20
Hypersensitivity reaction (all types)	190	98	Recovered = 125 Recovering = 15 Recovering with sequela = 1 Not recovered = 8 Unknown = 34 Fatal = 7
Severe hypotension	32	25	Recovered = 20 Recovering = 3 Unknown = 6 Fatal = 3
Severe cutaneous reaction	17	17	Recovered = 9 Recovering = 1 Not recovered = 2 Unknown = 3 Fatal = 2
Masking signs of inflammation	18	18	Recovered = 7 Recovering = 1 Not recovered = 3 Unknown = 3 Fatal = 4

^a Includes medically confirmed cases of each event through March 31, 2014.
GI = gastrointestinal.

CONCLUSIONS

- The occurrence of predefined safety events was relatively low with parecoxib considering nearly 70 million units were sold over a 12-year evaluation period, which is consistent with data from the clinical trial program.
- When administered according to the approved label, the overall benefit/risk assessment is considered favorable for parecoxib.

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