

[Letter to the Editor Response]

Thank you for the opportunity to respond to the points put forth by the reader regarding the use of SPRIX® (ketorolac tromethamine) nasal spray. As the developer of SPRIX®, the reader points out that prior pharmacokinetic data comparing oral with intramuscular (IM) ketorolac indicate that the time for the drug to reach maximum plasma concentration (t_{\max}) is as low as 20 minutes in fasted individuals² but may be slowed to 91 minutes in subjects after a high-fat breakfast.⁴ The reader also asserts that taking oral ketorolac on a full stomach is “a situation likely to occur in real-life settings” and, thus, a strong reason to favor the intranasal over the oral route of the drug. We agree that this certainly is a logical assertion. However, it must be kept in mind that the patient population of interest, specifically, professional football players in the National Football League (NFL), may not necessarily have had a high-fat content meal at the time of ketorolac use, as was studied by Mroszczak et al.⁴ Given the fact that these players are taking the medication either just prior to or during a game when a high-fat content meal would more likely hinder rather than help performance, it is more likely that the players’ stomachs would be nearly empty or, at most, contain merely clear liquids. There is no study, to our knowledge, that has evaluated the absorption kinetics of oral ketorolac taken in conjunction with clear liquids, such as sports drinks, commonly used prior to and during athletic competition.

The reader also points out that oral ketorolac (10 mg) is not indicated by the Food and Drug Administration (FDA) for first-line analgesic therapy since it was originally approved for use as continuation therapy following intravenous (IV) or IM dosing of ketorolac tromethamine. As mentioned in our article, we acknowledge that the use of oral ketorolac without prior IV or IM dosing is considered “off-label.” In our experience, the isolated use of oral ketorolac is quite common outside of the NFL for its analgesic properties following acute strains and sprains and overuse injuries and as an adjunct to narcotic medication. In addition, there have been no complications that we are aware of related to the isolated use of oral ketorolac within the appropriate dosing schedule of 10 mg every 4 to 6 hours, with a maximum of 40 mg per day, not to exceed 5 days.⁵ Because of the established safety and efficacy of the oral version of ketorolac, it is unlikely that further evaluation by the manufacturer or FDA will be conducted or is warranted. Nevertheless, each physician is to use his or her discretion as to the rational use of “off-label” medications.

We agree that there are significant potential benefits to intranasal ketorolac for an NFL player such as its time to reach

maximum serum concentration and its ability to be administered without an injection. This last factor is particularly relevant in terms of patient discomfort, potential needle site infection, and the overall negative public image associated with pregame injections in NFL players. However, it must be remembered that each container of SPRIX® must be kept refrigerated in an upright position prior to its first use⁶ and can only be used by a single player because of obvious hygiene-related issues associated with multidose metered dispensers. Both of these issues represent logistical hurdles for each team’s medical staff in terms of transportation and storage during away games. Clearly, a single prepackaged inventoried supply of oral ketorolac pills would be much more efficient in terms of transportation, storage, and multiple player dosing. In addition, the known side effects of nasal mucosal irritation and watery eyes¹ may make the intranasal formulation less tolerable to some players. Finally, an informal and unscientific assessment of pricing comparisons that we conducted found that a well-known national pharmacy chain quoted the following prices for each route of administration: 30 oral tablets (10 mg/tablet), \$36.99; 10 vials of IM/IV ketorolac (30 mg/mL), \$139.99; and a single bottle of SPRIX® nasal spray (8 metered doses per bottle of 15.75 mg/spray, 2 sprays/dose), \$229.79. Therefore, the approximate cost of 1 recommended dose is as follows: two 10-mg oral tablets, \$2.47; one 30-mg IM injection, \$13.99; and two 15.75-mg intranasal pumps, \$57.45. Thus, the intranasal route is considerably more expensive than the oral or IM/IV routes, which may be a significant consideration for some health care providers. Nevertheless, we recognize that some teams’ medical staffs may prefer intranasal ketorolac to either the oral or injectable forms for the reasons mentioned above. We feel that this is perfectly acceptable as long as the medication is used within the boundaries established by the FDA, the drug’s manufacturer, and the recommendations set forth in our article.³

Sincerely,

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