

Original Research Article

Comparison of Labour Induction Outcomes with Sublingual versus Oral Misoprostol at Term: A Retrospective Cohort Study

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ABSTRACT

Background: Misoprostol can be administered through several routes for cervical ripening and labour induction. Route-related differences in absorption may influence the amount of drug required and the time from induction to birth, while maternal and neonatal safety must remain central.

Objectives: To compare induction efficiency, mode of delivery, maternal and intrapartum fetal safety outcomes, and early neonatal outcomes among term pregnancies managed with sublingual or oral misoprostol.

Methods: This retrospective cohort study included 50 term pregnancy records, with 25 women in the sublingual group and 25 in the oral group. Each administration contained 50 µg misoprostol. The principal outcome was the induction-to-delivery interval. Secondary outcomes included number and cumulative dose of misoprostol, oxytocin augmentation, delivery mode, uterine hyperstimulation, tachysystole, fetal distress or non-reassuring fetal status leading to caesarean delivery, postpartum haemorrhage, birth weight, Apgar scores, and neonatal intensive care unit admission. Continuous variables were compared using Welch's t-test or the Mann-Whitney U test, while categorical variables were assessed using the chi-square test or Fisher's exact test.

Results: Baseline age, parity, gestational age, Bishop Score, and indications for induction were comparable between groups. The sublingual group required fewer doses (median 2 versus 3; $p=0.032$) and a lower cumulative dose (median 100 versus 150 µg; $p=0.032$). Mean induction-to-delivery interval was 13.85 ± 3.26 hours with sublingual administration and 20.14 ± 3.32 hours with oral administration (mean difference 6.29 hours; 95% CI 4.42-8.16; $p<0.001$). Caesarean delivery occurred in 5 (20%) and 6 (24%) women, respectively. Fetal distress or non-reassuring fetal status leading to caesarean delivery occurred in 2 (8%) women in each group. Hyperstimulation, tachysystole, postpartum haemorrhage, birth weight, Apgar scores, and neonatal intensive care unit admission did not differ significantly.

Conclusion: In this cohort, sublingual misoprostol was associated with a shorter induction-to-delivery interval and lower drug exposure than the oral route. Fetal distress or non-reassuring fetal status was recorded equally in both groups, and the study did not demonstrate a fetal safety advantage for either route. Current guideline-supported practice favours low-dose oral misoprostol were incorporated into institutional protocols; the present findings should not be interpreted as support for routine 50 µg sublingual administration.

Keywords: Cervical Ripening, Induction-To-Delivery Interval, Oxytocin Augmentation, Maternal Safety, Neonatal Outcome.

INTRODUCTION

Induction of labour is undertaken when continuing pregnancy is judged to carry

greater maternal or fetal risk than planned birth. At or beyond term, the decision is common but clinically consequential: the

method selected should promote cervical change and timely vaginal birth without increasing uterine hyperstimulation, operative delivery, or neonatal compromise. International guidance therefore places equal emphasis on effectiveness, safety, acceptability, and the capacity of the facility to monitor labour appropriately.^[1,2]

Misoprostol, a prostaglandin E1 analogue, is attractive in routine obstetric practice because it is inexpensive, stable at room temperature, and can be administered by several routes. Evidence for low-dose oral regimens is substantial, although the optimal dose and dosing interval continue to vary across protocols.^[3] Route is not a minor pharmacological detail. Swallowed oral misoprostol undergoes first-pass metabolism, whereas sublingual administration produces rapid absorption and higher systemic exposure, which may accelerate uterine response but can also raise concern about dose-related adverse effects.^[4]

Direct comparisons between sublingual and oral administration remain relatively limited. An earlier randomised trial found broadly similar effectiveness when the two routes were used at different doses, while a recent open-label trial using 50 µg by either route reported fewer doses and a shorter induction-to-delivery interval with sublingual administration.^[5,6] Wider meta-analytic evidence suggests that oral and sublingual regimens can both achieve effective induction, yet heterogeneity in dose, interval, clinical population, and comparator route makes local outcome assessment necessary.^[7]

This study was therefore designed to compare labour induction outcomes among term pregnancies receiving 50 µg misoprostol per administration through the sublingual or oral route. The primary objective was to compare the induction-to-delivery interval. Secondary objectives were to evaluate cumulative drug requirement, oxytocin augmentation, mode of delivery, maternal adverse events, and early neonatal outcomes.

MATERIALS AND METHODS

Study Design and Setting

A hospital-based retrospective cohort study was conducted in the Department of Obstetrics and Gynaecology for a period of one year in Chikkamagaluru Institute of Medical Sciences, Chikkamagaluru, Karnataka. The study compared two exposure groups

defined by the documented route of misoprostol administration: sublingual and oral.

Study Population and Sample Size

The analysed cohort comprised 50 term pregnancy records. Twenty-five women had received sublingual misoprostol and 25 had received oral misoprostol for labour induction.

Eligibility Criteria

Records were eligible when gestational age was between 37+0 and 41+6 weeks, misoprostol had been administered at 50 µg per dose through either the sublingual or oral route, and the record contained the principal induction and delivery outcomes. Records lacking documentation of route, dosage, induction-to-delivery interval, or delivery outcome were excluded.

Exposure and Outcome Assessment

The exposure of interest was the route of misoprostol administration. Across both groups, the dose per administration was 50 µg; the recorded number of doses ranged from one to three, producing cumulative doses of 50–150 µg. The principal outcome was the interval from initiation of induction to delivery, expressed in hours. Secondary effectiveness outcomes included number of doses, cumulative dose, oxytocin augmentation, delivery within 24 hours, and mode of delivery. Maternal safety outcomes comprised uterine hyperstimulation, tachysystole, shivering, and postpartum haemorrhage as recorded in the clinical record. The intrapartum fetal safety outcome was fetal distress or non-reassuring fetal status recorded as the indication for caesarean delivery. Neonatal outcomes were birth weight, one- and five-minute Apgar scores, five-minute Apgar score ≤ 7 , and neonatal intensive care unit admission.

Data Handling and Statistical Analysis

Continuous variables were summarised using mean $\pm$ standard deviation when treated as approximately continuous and median with interquartile range for ordinal or discrete measures. Categorical variables were expressed as frequencies and percentages. Between-group comparisons used Welch's independent-samples t-test for continuous variables, the Mann-Whitney U test for ordinal or non-normally distributed variables, the chi-square test for multi-category variables, and Fisher's exact test when expected cell counts

were small. The mean difference in induction-to-delivery interval was reported with a 95% confidence interval. All tests were two-sided, and $p < 0.05$ was considered statistically significant. Analysis was performed in Python using pandas and SciPy.

Ethical Considerations

The study involved a retrospective review of anonymised hospital records. There was no direct patient contact or alteration in clinical management. Patient confidentiality was maintained throughout, and all clinical information was handled in accordance with institutional ethical principles.

RESULTS

Baseline Characteristics

All 50 records were included, with 25 participants in each route group. Mean age was 29.16 ± 3.78 years in the sublingual group and 29.68 ± 4.09 years in the oral group. Both groups contained 10 nulliparous women (40%). Gestational age, parity, baseline Bishop score, and the distribution of indications for induction were closely matched (Table 1). Post-dates pregnancy was the most frequent indication in both groups, followed by prelabour rupture of membranes.

Characteristic	Sublingual (N=25)	Oral (N=25)	P-Value
Age (Years), Mean $\pm$ SD	29.16 $\pm$ 3.78	29.68 $\pm$ 4.09	0.643
Nulliparous, N (%)	10 (40.0)	10 (40.0)	1.000
Parity, Median (IQR)	1 (0–2)	1 (0–2)	1.000
Gestational Age (Weeks), Mean $\pm$ SD	39.58 $\pm$ 1.25	39.61 $\pm$ 1.30	0.950
Bishop Score, Median (IQR)	4 (3–4)	4 (3–4)	0.968
Indication For Induction, N (%)			1.000
Post-Dates	6 (24.0)	6 (24.0)	
Prelabour Rupture Of Membranes	5 (20.0)	5 (20.0)	
Hypertensive Disorders	3 (12.0)	3 (12.0)	
Gestational Diabetes	3 (12.0)	3 (12.0)	
Oligohydramnios	3 (12.0)	3 (12.0)	
Fetal Growth Restriction	3 (12.0)	3 (12.0)	
Elective	2 (8.0)	2 (8.0)	

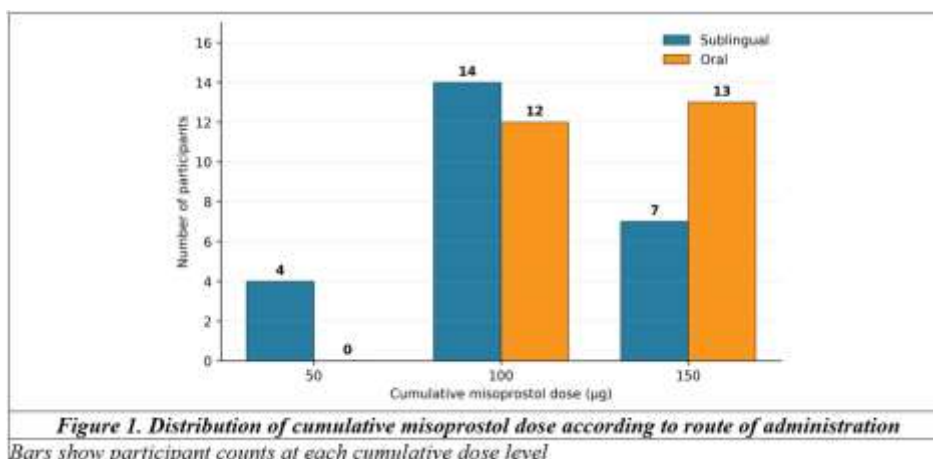
Table 1. Baseline Obstetric Characteristics and Indications for Induction (N=50)

SD: Standard Deviation; IQR: Interquartile Range. Continuous Variables Were Compared with Welch's T-Test Or Mann-Whitney U Test; Categorical Variables With Chi-Square Or Fisher's Exact Test, As Appropriate

Induction and delivery outcomes

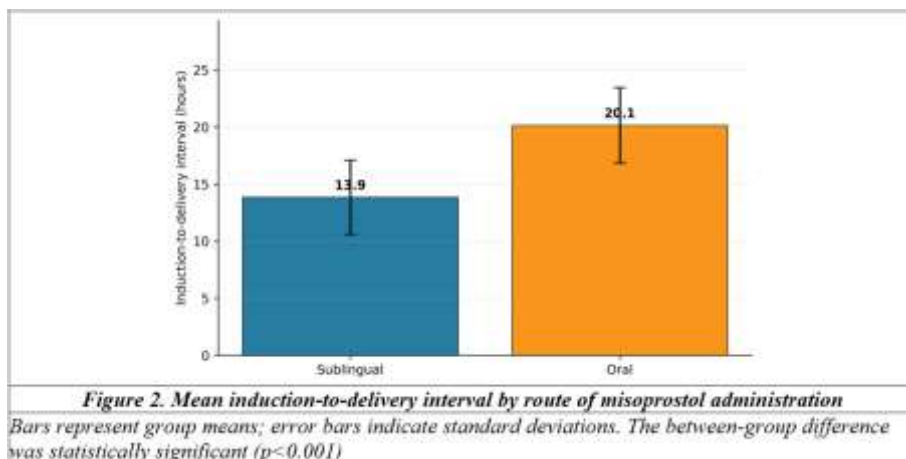
The sublingual group required fewer administrations than the oral group, with a median of 2 (IQR 2–3) versus 3 (IQR 2–3) doses ($p=0.032$). Cumulative exposure was correspondingly lower: median 100 μ g versus 150 μ g ($p=0.032$). Oxytocin augmentation

was required in 15 (60%) sublingual inductions and 19 (76%) oral inductions, a difference that was not statistically significant (Table 2). The cumulative dose distribution is displayed in Figure 1.



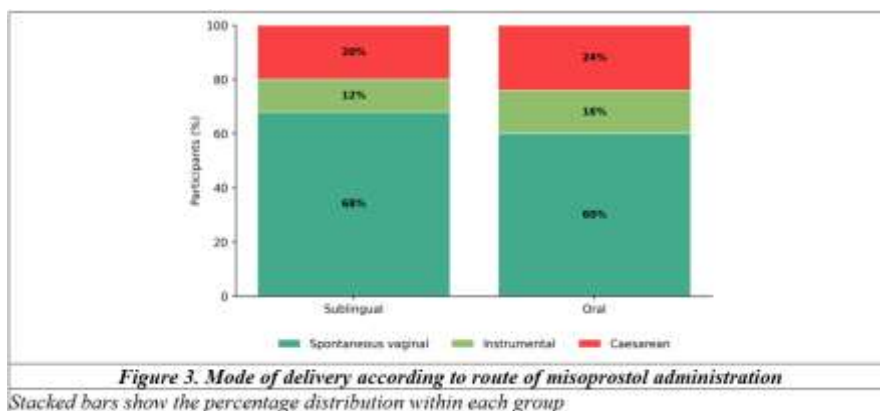
Mean induction-to-delivery interval was 13.85 ± 3.26 hours in the sublingual group and 20.14 ± 3.32 hours in the oral group. Sublingual administration shortened the interval by 6.29 hours (95% CI 4.42–8.16;

$p < 0.001$), as illustrated in Figure 2. Delivery occurred within 24 hours in all 25 sublingual cases and in 21 (84%) oral cases, although this categorical comparison did not reach statistical significance ($p = 0.110$).



Spontaneous vaginal delivery occurred in 17 (68%) women in the sublingual group and 15 (60%) in the oral group. Instrumental delivery occurred in 3 (12%) and 4 (16%), while caesarean delivery occurred in 5 (20%) and 6 (24%), respectively. The overall mode-of-

delivery distribution was similar ($p = 0.836$) (Figure 3). Failure to progress was the commonest recorded indication for caesarean delivery, accounting for 2 of 5 caesareans in the sublingual group and 3 of 6 in the oral group.



Outcome	Sublingual (N=25)	Oral (N=25)	P-Value
Number Of Doses, Median (IQR)	2 (2–3)	3 (2–3)	0.032
Cumulative Dose (µg), Median (IQR)	100 (100–150)	150 (100–150)	0.032
Oxytocin Augmentation, N (%)	15 (60.0)	19 (76.0)	0.364
Induction-To-Delivery Interval (Hours), Mean±SD	13.85 ± 3.26	20.14 ± 3.32	<0.001
Delivery Within 24 Hours, N (%)	25 (100.0)	21 (84.0)	0.110
Mode Of Delivery, N (%)			0.836
Spontaneous Vaginal	17 (68.0)	15 (60.0)	
Instrumental	3 (12.0)	4 (16.0)	
Caesarean	5 (20.0)	6 (24.0)	

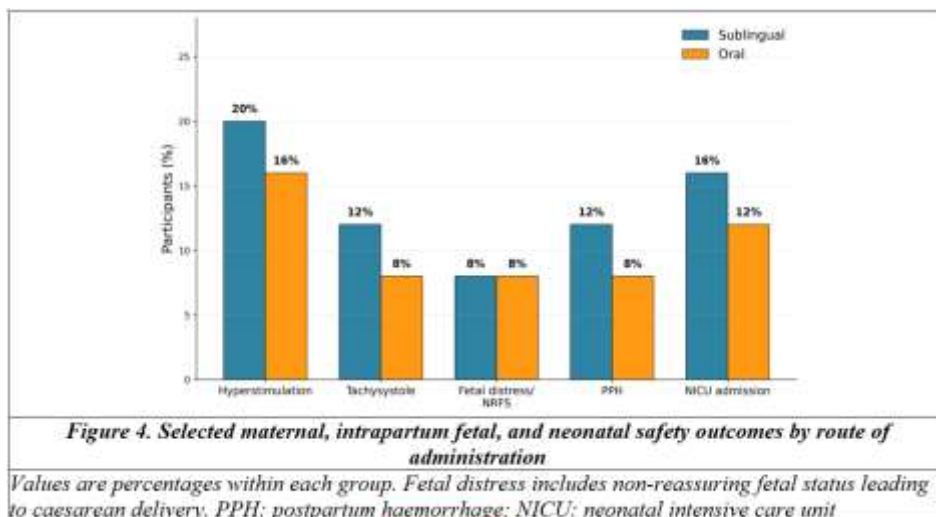
Table 2. Induction Process and Delivery Outcomes According to Administration Route

IQR: Interquartile Range; SD: Standard Deviation. The Mean Difference in Induction-To-Delivery Interval (Sublingual Minus Oral) Was –6.29 Hours (95% CI –8.16 To –4.42)

Maternal and intrapartum fetal safety outcomes

Selected maternal and intrapartum fetal safety outcomes did not differ significantly between groups (Table 3). Uterine hyperstimulation occurred in 5 (20%) women after sublingual administration and 4 (16%) after oral administration. Tachysystole occurred in 3 (12%) and 2 (8%), respectively. Fetal distress

or non-reassuring fetal status leading to caesarean delivery was documented in 2 (8%) women in each group. Postpartum haemorrhage occurred in 3 (12%) sublingual cases and 2 (8%) oral cases. These outcomes, together with neonatal intensive care unit admission, are displayed in Figure 4.



Safety Outcome, N (%)	Sublingual (N=25)	Oral (N=25)	P-Value
Uterine Hyperstimulation	5 (20.0)	4 (16.0)	1.000
Tachysystole	3 (12.0)	2 (8.0)	1.000
Fetal Distress/NRFS Prompting Caesarean Delivery	2 (8.0)	2 (8.0)	1.000
Shivering	4 (16.0)	2 (8.0)	0.667
Postpartum Haemorrhage	3 (12.0)	2 (8.0)	1.000
Any Selected Maternal Adverse Event	8 (32.0)	6 (24.0)	0.754

Table 3. Selected Maternal and Intrapartum Fetal Safety Outcomes According to Route of Misoprostol Administration

All Comparisons Used Fisher's Exact Test. Fetal Distress Includes Non-Reassuring Fetal Status Recorded as the Indication EOR Caesarean Delivery. "Any Selected Maternal Adverse Event" Denotes At Least One Episode of Uterine Hyperstimulation, Tachysystole, Shivering, or Postpartum Haemorrhage and Excludes Fetal Distress

Neonatal outcomes

Mean birth weight was 3168.0±384.8 g in the sublingual group and 3178.8±366.4 g in the oral group (p=0.919). Median one- and five-minute Apgar scores were comparable. Two

neonates (8%) in each group had a five-minute Apgar score ≤7. Neonatal intensive care unit admission occurred in 4 (16%) versus 3 (12%) neonates (p=1.000) (Table 4).

Outcome	Sublingual (N=25)	Oral (N=25)	P-Value
Birth Weight (G), Mean±SD	3168.0 ± 384.8	3178.8 ± 366.4	0.919
Apgar Score At 1 Minute, Median (IQR)	8 (8–9)	8 (8–9)	0.942
Apgar Score At 5 Minutes, Median (IQR)	9 (9–9)	9 (9–9)	0.853
Five-Minute Apgar Score ≤7, N (%)	2 (8.0)	2 (8.0)	1.000
NICU Admission, N (%)	4 (16.0)	3 (12.0)	1.000

Table 4. Early Neonatal Outcomes According to Route of Misoprostol Administration

SD: Standard Deviation; IQR: Interquartile Range; NICU: Neonatal Intensive Care Unit

DISCUSSION

The principal finding was a substantially shorter induction-to-delivery interval with sublingual misoprostol. The average reduction was 6.29 hours, and this occurred alongside fewer administrations and a lower cumulative dose. These efficiency gains did not translate into a detectable difference in spontaneous vaginal birth, instrumental delivery, caesarean delivery, fetal distress or non-reassuring fetal status leading to caesarean delivery, or the measured maternal and early neonatal outcomes. For a busy labour ward, the time difference is clinically relevant. Yet the absence of a safety signal in 25 women per group should not be interpreted as evidence that uncommon complications are equivalent. The direction of the findings is consistent with the two direct route-comparison trials most relevant to this question. Shetty et al. reported broadly comparable induction outcomes with sublingual and oral misoprostol, although the doses were not equivalent between groups.^[5] More recently, Datta et al. used 50 µg in both groups and found that sublingual administration required fewer doses and shortened the induction-to-delivery interval, while mode of delivery and short-term safety outcomes remained comparable.^[6] The present cohort follows the same pattern, with the advantage that both groups received an identical 50-µg dose per administration, though the retrospective design cannot account fully for clinical selection of route.

A pharmacokinetic explanation is plausible. Sublingual administration avoids swallowing and first-pass hepatic metabolism, producing rapid absorption and greater bioavailability than the conventional oral route.^[4] A faster and more sustained systemic concentration can intensify cervical and uterine response, thereby reducing the amount of drug and elapsed time required. The same mechanism, however, is also the reason dose and monitoring matter. Faster exposure may increase uterine activity in susceptible women, so efficiency should never be separated from surveillance of contractions and fetal status.

The observed delivery modes were reassuringly similar. Caesarean delivery occurred in one-fifth of the sublingual group and slightly less than one-quarter of the oral group, with failure to progress the leading indication. The study was not powered to establish non-inferiority, but the pattern does not suggest that the shorter interval was purchased at the cost of more operative birth.

Meta-analytic evidence comparing oral or sublingual misoprostol with vaginal regimens has likewise found that route can influence time-related outcomes without a consistent increase in maternal or neonatal morbidity.^[7]

Trials of sublingual versus vaginal administration have produced mixed results: some report more rapid induction, while others highlight a possible increase in tachysystole or hyperstimulation at higher exposure.^[8-10] This variability reinforces the importance of interpreting route together with dose, dosing interval, parity, cervical status, and the indication for induction.

The safety findings require measured interpretation. Hyperstimulation, tachysystole, shivering, postpartum haemorrhage, low five-minute Apgar score, neonatal intensive care unit admission, and fetal distress or non-reassuring fetal status leading to caesarean delivery were statistically comparable. The fetal distress outcome occurred in 2 (8%) women in each group; therefore, the present records do not demonstrate a higher fetal distress rate with the sublingual route or a fetal safety advantage with the oral route. Still, the confidence available from a cohort of 50 is limited. Older systematic reviews and route-specific trials have repeatedly noted that uterine hyperstimulation is sensitive to regimen intensity.^[8,11-13] Contemporary reviews of oral induction commonly favour lower starting doses, often 25 µg or less, because the objective is a controllable uterine response rather than maximal speed.^[3,11] The 50-µg administrations documented here therefore describe local clinical practice and should not be read as a universal dosing recommendation.

The results are relevant to Indian obstetric services, where misoprostol is frequently valued for low cost, ease of storage, and practical administration. A reduction of several hours in the induction-to-delivery interval could ease bed occupancy and reduce prolonged labour-room observation, particularly in high-volume public hospitals. Other Indian trials of oral misoprostol have similarly emphasised that effectiveness must be balanced against protocol discipline and timely escalation when induction is unsuccessful.^[14,15] Current NICE guidance includes low-dose oral misoprostol 25 µg among the options for cervical ripening in women with an unfavourable cervix, while WHO guidance recommends 25 µg oral misoprostol at 2-hour intervals.^[16,17]

Accordingly, where local policy follows these regimens, low-dose oral administration may be preferred over the 50 µg sublingual regimen evaluated here. These recommendations do not establish oral misoprostol as the only acceptable induction method; route selection remains dependent on the approved formulation, institutional protocol, patient characteristics, and capacity for fetal and uterine monitoring.

Strengths and limitations

The study compared equal per-administration doses and used clinically meaningful maternal, intrapartum fetal, and neonatal outcomes. Baseline age, parity, gestational age, Bishop score, and indications were closely balanced, which supports a fair descriptive comparison. Several limitations remain. The retrospective, single-department design permits selection bias and residual confounding because route allocation was not random. The sample was small, particularly for uncommon adverse events and fetal distress. Exact dosing intervals, body mass index, detailed membrane status, fetal presentation, previous uterine surgery, cardiotocographic findings, and clinician-level decision factors were not available for adjustment. Fetal distress was identified only when documented as an indication for caesarean delivery; less severe or transient fetal heart-rate abnormalities may therefore have been missed. Recorded adverse events depended on the completeness of routine documentation, and longer-term neonatal outcomes were not assessed. These limitations restrict causal interpretation and generalisability.

CONCLUSION

Sublingual administration of 50 µg misoprostol per dose was associated with fewer doses, lower cumulative exposure, and a markedly shorter induction-to-delivery interval than oral administration in this retrospective term cohort. Fetal distress or non-reassuring fetal status leading to caesarean delivery occurred equally in both groups, and the study did not establish a fetal safety advantage for either route. In view of guideline-supported low-dose oral regimens, oral misoprostol may be preferred where adopted within an approved institutional induction protocol. The findings do not support an oral-only recommendation and should not be extrapolated to endorse routine 50 µg sublingual administration without larger prospective safety data.

DECLARATIONS

Source of Funding

Nil.

Conflict of Interest

None declared.

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