No. 432c, January 2023 (Replaces No. 296, September 2013)

Guideline No. 432c: Induction of Labour

(En français : Directive clinique n^{o} 432c : Déclenchement artificiel du travail)

The English document is the original version. In the event of any discrepancy between the English and French content, the English version prevails.

This clinical practice guideline was prepared by the authors and overseen by the SOGC Clinical Practice – Obstetrics Committee. It was reviewed by the SOGC Obstetrical Content Review Committee. It was reviewed and approved by the SOGC Guideline Management and Oversight Committee and the SOGC Board of Directors.

This clinical practice guideline supersedes No. 296, published in September 2013.

Authors

debbie Robinson, MD, Winnipeg, MB
Kim Campbell, RM, Vancouver, BC
Sebastian R. Hobson, MD, PhD, Toronto, ON
W. Kim MacDonald, MD, Victoria, BC
Diane Sawchuck, RN, PhD, Victoria, BC
Brenda Wagner, MD, Vancouver, BC

Disclosures: Statements were received from all authors. No relationships or activities that could involve a conflict of interest were declared. All authors have indicated that they meet the journal's requirements for authorship.

Weeks Gestation Notation: The authors follow the World Health Organization's notation on gestational age: the first day of the last menstrual period is day 0 (of week 0); therefore, days 0 to 6 correspond to completed week 0, days 7 to 13 correspond to completed week 1, etc.

Key Words: induction; labour; cervical ripening

Corresponding Author: debbie Robinson, debbie.Robinson@umanitoba.ca

KEY MESSAGE

1. Oral misoprostol in a titratable fashion or oxytocin with amniotomy is the preferred method of induction of labour when the Bishop score is 7 or greater.

J Obstet Gynaecol Can 2023;45(1):70–7

https://doi.org/10.1016/j.jogc.2022.11.009

ABSTRACT

Objectives: This guideline presents evidence and recommendations for cervical ripening and induction of labour. It aims to provide information to birth attendants and pregnant individuals on optimal perinatal care while avoiding unnecessary obstetrical intervention.

Target Population: All pregnant patients.

Benefits, Risks, and Costs: Consistent interprofessional use of the guideline, appropriate equipment, and trained professional staff enhance safe intrapartum care. Pregnant individuals and their support person(s) should be informed of the benefits and risks of induction of labour.

Evidence: Literature published to March 2022 was reviewed. PubMed, CINAHL, and the Cochrane Library were used to search for systematic reviews, randomized control trials, and observational studies on cervical ripening and induction labour. Grey (unpublished) literature was identified by searching the websites of health technology assessment and health technology related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Validation Methods: The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. See online Appendix A (Tables A1 for definitions and A2 for interpretations of strong and conditional [weak] recommendations).

Intended Audience: All providers of obstetrical care.

SUMMARY STATEMENTS

Misoprostol

1. Oral misoprostol is both as or more effective and safe than other methods of induction of labour. Misoprostol in solution is easy to prepare and administer, has an advantageous 2 hour half-life, and allows for titratable dosing while maintaining a maximum dose in the low dose range ($\leq$ 50 μg) (*high*).
2. Like oxytocin, there is no single best dose of misoprostol. The dose should be started at 20−25 μg and titrated to contractions, allowing each patient to have a customized regimen (*moderate*).
3. Continuous electronic fetal monitoring (EFM) is recommended for at least 20 minutes post administration. If there are no signs of active labour after 30 minutes, encourage patient ambulation until the next dose (*moderate*).
4. When signs of active labour present, establish EFM. Continue ambulation as per fetal health surveillance guidelines (*high*).
5. Consider intravenous (IV) access once the patient is in active labour (*moderate*).
6. Once active labour has commenced and/or once the membranes are ruptured, the clinician is not required to switch from misoprostol to oxytocin, as continuing with misoprostol may be more effective (*high*).

Oxytocin

1. Oxytocin can increase the risk of postpartum hemorrhage, volume overload, and/or hyponatremia with prolonged or high maximal dose use (*high*).
2. There are no data to support maintaining the rate of oxytocin at any particular dose threshold rather than continuing the titration every 30 minutes when contractions are not adequate. Consider an intrauterine pressure catheter if contractions are difficult to monitor. Ongoing diligence by the most responsible physician is required when titrating oxytocin at any rate (*moderate*).
3. Caution is needed when using oxytocin in a patient with previous cesarean delivery or uterine surgery (*high*).
4. Reducing the rate of oxytocin infusion after achieving active labour and cervical dilation of at least 5 cm may be considered (*low*).

RECOMMENDATIONS

1. Oral prostaglandin E_1 or intravenous oxytocin with amniotomy is the preferred method of induction of labour when the Bishop score is 7 or greater (*strong, high*).
2. Health care providers can use prostaglandin E_1 concurrently with, or sequentially after, insertion of a balloon catheter (*strong, moderate*).
3. Health care providers may use prostaglandin E_2 gel or insert to induce labour when the Bishop score is 7 or greater (*strong, moderate*).
4. Health care providers may perform an amniotomy once the modified Bishop score is 7 or greater (*strong, high*). An amniotomy is most effective when combined with an induction agent (oxytocin or prostaglandin E_1) (*strong, high*).
4. Health care providers may perform an amniotomy once the modified Bishop score is 7 or greater (*strong, high*). An amniotomy is most effective when combined with an induction agent (oxytocin or prostaglandin E_1) (*strong, high*).
5. Health care providers should only use oxytocin for induction of labour when the modified Bishop score is 7 or greater, except in the setting of term pre-labour rupture of membranes (*strong, moderate*). Oxytocin is best combined with amniotomy (*strong, high*).
6. Health care providers should record oxytocin infusion rates in mU/min (*strong, moderate*).
7. A local institutional protocol for oxytocin use with a safety checklist is required, regardless of infusion rate (*strong, moderate*).
8. Health care providers should start oxytocin no earlier than: 30 minutes post prostaglandin E_2 vaginal insert removal, 6 hours post prostaglandin E_2 vaginal gel insertion, 2 hours post oral prostaglandin E_1, and 4 hours post vaginal prostaglandin E_1 insertion (*strong, high*).
9. Electronic fetal monitoring is recommended when using oxytocin or repeated doses of prostaglandin E_1 for induction of labour (*strong, high*).

INTRODUCTION

There are several options for induction of labour (IOL) with intact membranes and a Bishop score of 7 or greater.

These options include:

- prostaglandin E_1 (PGE_1)
- oxytocin with amniotomy
- prostaglandin E_2 (PGE_2)

Refer to Table 1 for a comparison summary of labour induction agents.

A best practice decision tree is modelled in the Figure.

For IOL with term pre-labour rupture of membranes (PROM), refer to Guideline No. 432a: Cervical Ripening and Induction of Labour — General Information.

The 2021 Cochrane systematic review and meta-analysis for induction of labour (IOL) states:

"The best available evidence suggests that low-dose oral misoprostol probably has many benefits over other methods for labour induction. This review supports the use of low-dose oral misoprostol for induction of labour, and demonstrates the lower risks of hyperstimulation than when misoprostol is given vaginally. More trials are needed to establish the optimum oral misoprostol regimen, but these findings suggest that a starting dose of 25 μg may offer a good balance of efficacy and safety."[1]

MISOPROSTOL

Misoprostol (PGE_1) is a highly effective pharmacologic agent for both cervical ripening and induction of labour. The use of medications for off-label purposes is legally permitted in Canada provided that the proposed use has been well-researched, there is peer support for the indication, and the risks and benefits of the proposed treatment have been discussed with the patient. Misoprostol has been studied in >100 000 pregnancies, has been used worldwide for >15 years, and is recommended in other international IOL guidelines. Therefore, misoprostol should be included as part of the informed decision-making process for induction of labour.

There is a plethora of data on misoprostol (oral tablets, oral solution, vaginal, and sublingual) compared with placebo, mechanical options, dinoprostone (both gel and insert), and oxytocin for induction of labour. A summary of the salient findings and reports is presented in this guideline.

The Royal College of Physicians and Surgeons of Canada CanMEDS framework lists financial responsibility as part of the "Leader" role. As such, it should be noted that misoprostol, with favourable efficacy and safety compared to other induction methods, is the most economical of all induction agents.[2,3]

Absolute contraindications to PGE_1 use include:

- Previous full thickness uterine surgery[4]
- Known fetal compromise

Oral Misoprostol versus Alternatives in All Settings

A 2021 Cochrane review of 61 trials (n = 20 026), which did not differentiate between membrane status or Bishop score, compared oral misoprostol with placebo (4 trials; n = 594), dinoprostone (13 trials; n = 9676), vaginal misoprostol (33 trials; n = 6110), oxytocin (6 trials; n = 737 200 with rupture of membranes), or mechanical methods (6 trials; n = 2993).[1] In all comparisons, oral misoprostol was at least as effective and safe as oxytocin, dinoprostone, and vaginal misoprostol, and in some cases superior. Overall, the researchers concluded that low dose oral misoprostol every 2 hours appears to be a safe and effective method of induction when compared with all alternatives.

Oral Misoprostol in Solution

The small doses of misoprostol required to induce labour can be challenging to administer accurately. Rapidly dissolvable in plain water, misoprostol in solution is stable for 24 hours[5] and provides accurate and titratable oral dosing. Pharmacokinetics and clinical trials support a q2h dosing frequency.[6] The dose can be increased if repeated lower doses are unsuccessful at achieving labour;

ABBREVIATIONS

CD	cesarean delivery
EFM	electronic fetal monitoring
FHR	fetal heart rate
IOL	induction of labour
IV	intravenous
PGE_1	prostaglandin E_1
PGE_2	prostaglandin E_2
PROM	pre-labour rupture of membranes
TOLAC	trial of labour after cesarean

Table 1. Comparison Summary of Labour Induction Agents

Induction Agent	Dose	Efficacy - Delivery within 24 hours [a]	Risk of Tachysystole	Efficacy with term PROM	Safety with TOLAC
PGE_1 Soln	10–50 μg q2h	High	Moderate	High	No
PGE_1 PO	25–50 μg q4h	High	Moderate	High	No
PGE_1 with Balloon	10–50 μg q2h or 50 μg q4h	High (starting with BS <7)	Moderate	N/A	No
PGE_1 Vaginal	25–50 μg q4h	High	High	High	No
PGE_2 Gel	2 mg q6h	High	Moderate	Moderate	No
PGE_2 Mesh	10 mg q12–24h	Moderate	Moderate	Moderate	No
Oxytocin with Balloon	1–40 mU/minute	Moderate (starting with BS <7)	Moderate	N/A	Yes
Oxytocin with Amniotomy	1–40 mU/minute	High	Moderate	N/A	Yes
Oxytocin Alone	1–40 mU/minute	Low	Moderate	High	Yes

[a]starting with a modified Bishop score (BS) of seven or greater unless otherwise stated or term PROM

however, the dose should not exceed 50 μg. If labour has not been successfully achieved by 24 hours, an alternate plan for IOL should be considered. Like oxytocin, there is no "right dose," rather the dose must be titrated to contractions. **The recurring question of what the optimal dosing regimen should be is addressed by a titratable protocol, starting at 20 μg and increasing q2h, which can tailor the dose for each individual labour.**

Refer to Appendix B for instructions on preparing the oral misoprostol solution, Appendix C for a sample protocol, and Appendix D for a sample protocol worksheet.

Oral Misoprostol in Solution versus Alternatives in All Settings

In 2015, Alfirevic et al. published a meta-analysis of 280 randomized controlled trials (n = 48 068) of all prostaglandins for labour induction. The results were inconclusive due to wide confidence intervals. However, it appeared that low dose (<50 μg) titrated oral misoprostol solution may have the lowest probability of cesarean delivery (CD).[7]

A retrospective cohort (n = 4000) in 2017 comparing titrated oral misoprostol dosed q2h with all other methods of cervical ripening and IOL, reported a CD rate of 17% in the misoprostol group versus 26% for other methods (PGE_2, balloon, oxytocin) ($P < 0.001$). There was no difference in the cord blood acid-base status, Apgar score, or postpartum hemorrhage.[8]

Oral Misoprostol in Solution versus Oxytocin with a Favourable Bishop Score

A 2019 double-blind, randomized, controlled trial comparing titrated oral misoprostol (dosed q2h and increased as needed) with oxytocin when the Bishop score was >5, reported that while contractions started sooner in the oxytocin group (69.7 minutes vs. 262 minutes; $P < .001$), the misoprostol group demonstrated more deliveries within 12 hours (57% vs. 35%, $P = .04$) and within 24 hours (100% vs. 90%, $P = .04$).[9] Tachysystole and meconium staining were more frequent in the misoprostol group (15% vs. 1%; $P = .04$ and 20% vs. 5%; $P = .04$, respectively); however, these did not translate into higher CD rates, or into any adverse maternal or perinatal outcomes. Maternal and fetal efficacy and safety were equivalent in both groups.

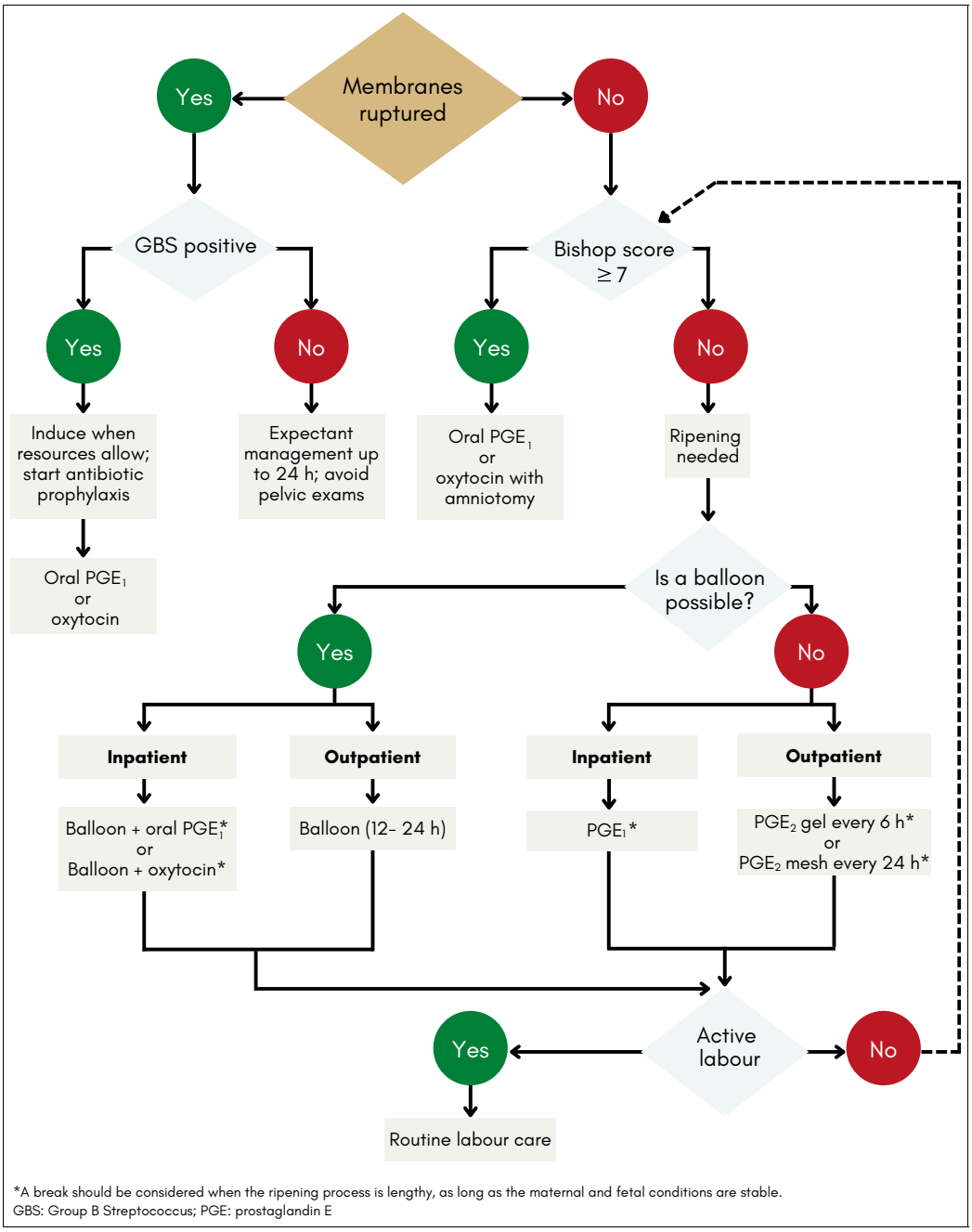
Oral Misoprostol in Solution versus Dinoprostone with a Favourable Bishop Score

A 2017 randomized controlled trial compared titrated oral misoprostol with dinoprostone as an IOL agent (rather than as a ripening agent) in 212 individuals with a Bishop score of up to 8.[10] Overall, the misoprostol group had a longer induction to delivery interval (975 minutes vs. 670 minutes, $P = .01$); however, the researchers reported a higher delivery rate at 24 hours (92.6% vs. 79.8%; $P = .01$). The dinoprostone group had a higher rate of oxytocin augmentation (38% vs. 10.6%; $P < .01$). Maternal and perinatal outcomes were equivalent in all other respects, with no concerns for safety or efficacy in either group.

Vaginal Misoprostol versus Other Induction Methods

The 2015 Alfirevic et al. review of 210 trials (n = 48 068) found that the odds of failing to achieve a vaginal delivery within 24 hours were lowest with vaginal misoprostol (≥50 μg) (OR 0.06; 95% CI 0.02–0.12); however, this route had higher rates of uterine tachysystole.[7] The odds of cesarean delivery were lowest with titrated oral misoprostol solution (<50 μg) (OR 0.65; 95% CI 0.49–0.83),

Figure.



with lower rates of uterine tachysystole. This review concluded that no further trials should be done on vaginal misoprostol as the oral route was superior.

Sublingual Misoprostol

Sublingual misoprostol appears to have similar efficacy to the oral route. A systematic review of 5 studies (n = 740) found no difference in vaginal deliveries at 24 hours, uterine tachysystole, or cesarean delivery rate whether misoprostol 25–50 μg was given sublingually or vaginally.[11] Patient satisfaction was higher with the sublingual route compared to the vaginal route.[12,13]

Amniotomy with Misoprostol Use

The current evidence does not address if IOL with misoprostol benefits from concurrent amniotomy. Some previous studies included amniotomy when the Bishop score was 8 or greater; however, the relationship between amniotomy

Table 2. Low-Rate versus Expedited-Rate Oxytocin Protocol

Oxytocin Properties	Low-Rate Protocol	Expedited-Rate Protocol
Initial dose of oxytocin	1–2 mU/minute	4–6 mU/minute
Increase interval	30 minutes	30 minutes
Dosage increment	1–2 mU	4–6 mU
Benefits	Less tachysystole Lower total dose	Shorter time to delivery
Risks	Longer time to delivery	More tachysystole with or without FHR changes
Relative contraindications		TOLAC, parity ≥5, second stage, augmentation of labour

and misoprostol was not specifically evaluated. Clinicians may consider amniotomy once there is commitment to delivery, as this procedure may augment the induction process.

AMNIOTOMY

There is limited evidence to support amniotomy alone as a method of IOL.[14] Amniotomy commits patients to delivery and when used independent of another IOL agent, it is associated with a longer time to birth, higher rates of infection, and possibly an increase in CD rates.[15] It is more successful in multiparous patients with a favourable Bishop score, and is best followed by early use of PGE_1 or oxytocin.

Amniotomy combined with another method of IOL (PGE_1, PGE_2, or oxytocin) may decrease the intervention-to-birth interval.[16] However, in individuals with an elevated BMI, early amniotomy increases the risk of CD in proportion to the BMI. Therefore, the higher the BMI, the higher the rate of CD with early amniotomy.[17] Amniotomy at <4 cm dilation may increase the CD rate in patients undergoing a trial of labour after cesarean (TOLAC).[18] If an amniotomy is indicated with an unengaged presenting part, the surgical team and the operating room should be immediately available in case of cord prolapse requiring an emergency CD.

OXYTOCIN

Oxytocin is a hormone that binds to uterine receptors to produce contractions. Oxytocin is administered as a controlled IV infusion for IOL, and has a half-life of 1–6 minutes and a time to steady plasma concentration of 40 minutes.[19] It has no direct effects on the cervix. Synthetic oxytocin does not cross the maternal blood brain barrier, which may influence the individual's perception of pain in labour.[20] The uterus is increasingly responsive to oxytocin as pregnancy progresses and decreasingly responsive with prolonged labour due to the saturation of receptors. Volume overload and hyponatremia may occur with high doses (>40 mU/minute) or prolonged infusions. Continuous EFM should be utilised with oxytocin infusions due to the risk of uterine tachysystole with fetal heart rate (FHR) changes. If both maternal and fetal status are normal, and the oxytocin is at a stable rate, breaks in continuous EFM of up to 30 minutes, with an intermittent auscultation check at 15 minutes, may be given to encourage ambulation and other activities.[21] The ideal dosing regimen of oxytocin should be individualised and titrated to uterine activity, and thus accurate uterine activity assessment is essential. Both low-rate and expedited-rate protocols may be used (see Table 2). We suggest the terms "low-rate" and "expedited-rate" as preferred alternatives to "low-dose" and "high-dose" as these terms are misleading. The actual dose of oxytocin is the same in both regimens, only the time to reach that dose is altered.

Institutions may choose to have policies addressing how often reassessment or consultation by the most responsible physician should occur. Because solution concentrations vary, the rate of infusion should always be documented in mU/minute rather than mL/hour.

Oxytocin is a high alert medication as per the Institute for Safe Medication Practices Canada (ISMP Canada). It has a heightened risk of causing significant patient harm when used inappropriately. Oxytocin requires the use of independent double-checks where 2 individuals, separately, and independently of each other, check a process in the workflow. This check is performed:

- when adding oxytocin to an IV infusion bag;
- when setting the initial infusion rate with the infusion pump medication program calculator;
- at shift change to confirm solution concentration and rate of administration.

Outside the setting of term PROM, oxytocin alone should only be used when the Bishop score is greater than 7. For

Table 3. Risk of Uterine Rupture with Oxytocin Use and Prior Uterine Surgery

Labour Outcome	Oxytocin Use	Spontaneous Labour	*P* value
Successful vaginal birth after cesarean (VBAC)	60.7%	74.3%	0.001
Rupture	2.2%	0.7%	0.0003

all individuals with an unfavourable Bishop score, regardless of membrane status, CD rates are increased when labour is induced with oxytocin alone.[14] A meta-analysis of 61 studies (n = 12 819) reported that oxytocin alone was associated with an increase in operative birth within 24 hours when compared with vaginal or intracervical prostaglandins (70% vs. 21%, and 51% vs. 35%, respectively). Early amniotomy after starting oxytocin is associated with shorter IOL to delivery intervals. [2,22]

Oxytocin with Foley Catheter

There is inconsistent evidence whether there is a difference in efficacy between the use of oxytocin concurrently with, or sequentially after, a cervical ripening balloon.[23,24] Since either option is safe, local resources, and the desire for outpatient versus inpatient management should guide decision making.

Decreasing Oxytocin During Induction

A 2018 Cochrane review examined the approach of discontinuing oxytocin once active labour was established and the cervix was at least 5 cm dilated.[25] The researchers reported a reduction in both CD and in uterine tachysystole with a small increase in the mean duration of the active phase of labour of less than 30 minutes. There is insufficient evidence to recommend either reducing or maintaining oxytocin when labour is actively progressing and the FHR is normal.

Trial of Labour after Cesarean and Uterine Rupture

Trial of labour after cesarean (TOLAC) is a risk factor for uterine rupture. Rarely, uterine rupture can occur in an unscarred uterus receiving oxytocin or in individuals with no previous uterine surgery in spontaneous labour.[26] Although oxytocin can increase the risk of uterine rupture somewhat, it is the safest method of IOL with prior uterine surgery (see Table 3).[27]

DINOPROSTONE (PGE_2)

As demonstrated in the trials of dinoprostone versus misoprostol above, dinoprostone gel or insert may be used as an induction agent when the Bishop score is greater than 7. The safety and efficacy profiles of both dinoprostone and misoprostol are satisfactory, although misoprostol may have some advantages.[6,10]

CONCLUSION

Once the Bishop score is 7 or greater, induction of labour is best accomplished by oral misoprostol or oxytocin with early amniotomy. Both agents should be titrated to contractions. Misoprostol may have the advantages of cost savings and lower cesarean delivery rates with equivalent or better neonatal outcomes than oxytocin. Both agents may be used concurrently with a Foley catheter, but only oxytocin should be considered in a patient with a previous cesarean delivery.

REFERENCES

1. Kerr RS, Kumar N, Williams MJ, et al. Low-dose oral misoprostol for induction of labour. Cochrane Database Syst Rev 2021;6:CD014484.
2. Alfirevic Z, Keeney E, Dowswell T, et al. Which method is best for the induction of labour? A systematic review, network meta-analysis and cost-effectiveness analysis. Health Technol Assess 2016;20:1–584.
3. Chatsis V, Frey N. CADTH rapid response reports. Misoprostol for cervical ripening and induction of labour: a review of clinical effectiveness, cost-effectiveness and guidelines. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2018.
4. Dy J, DeMeester S, Lipworth H, et al. No. 382-trial of labour after caesarean. J Obstet Gynaecol Can 2019;41:992–1011.
5. Alfirevic Z, Aflaifel N, Weeks A. Oral misoprostol for induction of labour. Cochrane Database Syst Rev 2014;2014:CD001338.
6. Wang X, Yang A, Ma Q, et al. Comparative study of titrated oral misoprostol solution and vaginal dinoprostone for labor induction at term pregnancy. Arch Gynecol Obstet 2016;294:495–503.
7. Alfirevic Z, Keeney E, Dowswell T, et al. Labour induction with prostaglandins: a systematic review and network meta-analysis. BMJ 2015;350:h217.
8. Wallstrom T, Jarnbert-Pettersson H, Stenson D, et al. Labor induction with orally administrated misoprostol: a retrospective cohort study. Biomed Res Int 2017;2017:6840592.
9. Kashanian M, Eshraghi N, Rahimi M, et al. Efficacy comparison of titrated oral solution of misoprostol and intravenous oxytocin on labour induction in women with full-term pregnancy. J Obstet Gynaecol 2020;40:20–4.
10. Yehia AH, Abd El Fattah I, Bayoumy KM, et al. Titrated misoprostol versus dinoprostone for labor induction. J Basic Clin Reprod Sci 2016;5:75–81.
11. Souza AS, Amorim MM, Feitosa FE. Comparison of sublingual versus vaginal misoprostol for the induction of labour: a systematic review. BJOG 2008;115:1340–9.

12. Nassar AH, Awwad J, Khalil AM, et al. A randomised comparison of patient satisfaction with vaginal and sublingual misoprostol for induction of labour at term. BJOG 2007;114:1215–21.

13. Zahran KM, Shahin AY, Abdellah MS, et al. Sublingual versus vaginal misoprostol for induction of labor at term: a randomized prospective placebo-controlled study. J Obstet Gynaecol Res 2009;35:1054–60.

14. Alfirevic Z, Kelly AJ, Dowswell T. Intravenous oxytocin alone for cervical ripening and induction of labour. Cochrane Database Syst Rev 2009;2009:CD003246.

15. Battarbee AN, Sandoval G, Grobman WA, et al. Maternal and neonatal outcomes associated with amniotomy among nulliparous women undergoing labor induction at term. Am J Perinatol 2021;38:e239–48.

16. Battarbee AN, Palatnik A, Peress DA, et al. Association of early amniotomy after foley balloon catheter ripening and duration of nulliparous labor induction. Obstet Gynecol 2016;128:592–7.

17. Battarbee AN, Glover AV, Stamilio DM. Association between early amniotomy in labour induction and severe maternal and neonatal morbidity. Aust N Z J Obstet Gynaecol 2020;60:108–14.

18. Varvoutis MS, Sayres LC, Dotters-Katz SK. Is early amniotomy associated with higher likelihood of vaginal birth after cesarean? AJP Rep 2020;10:e37–41.

19. Drugbank online. Oxytocin. Available at: https://go.drugbank.com/drugs/DB00107. Accessed on September 16, 2022.

20. Bell AF, Erickson EN, Carter CS. Beyond labor: the role of natural and synthetic oxytocin in the transition to motherhood. J Midwifery Womens Health 2014;59:35–42: quiz 108.

21. Dore S, Ehman W. No. 396-fetal health surveillance: intrapartum consensus guideline. J Obstet Gynaecol Can 2020;42:316–348.e9.

22. Selo-Ojeme DO, Pisal P, Lawal O, et al. A randomised controlled trial of amniotomy and immediate oxytocin infusion versus amniotomy and delayed oxytocin infusion for induction of labour at term. Arch Gynecol Obstet 2009;279:813–20.

23. Pettker CM, Pocock SB, Smok DP, et al. Transcervical foley catheter with and without oxytocin for cervical ripening: a randomized controlled trial. Obstet Gynecol 2008;111:1320–6.

24. Schoen CN, Grant G, Berghella V, et al. Intracervical foley catheter with and without oxytocin for labor induction: a randomized controlled trial. Obstet Gynecol 2017;129:1046–53.

25. Boie S, Glavind J, Velu AV, et al. Discontinuation of intravenous oxytocin in the active phase of induced labour. Cochrane Database Syst Rev 2018;8:CD012274.

26. Vernekar M, Rajib R. Unscarred uterine rupture: a retrospective analysis. J Obstet Gynaecol India 2016;66:51–4.

27. Zhang H, Liu H, Luo S, et al. Oxytocin use in trial of labor after cesarean and its relationship with risk of uterine rupture in women with one previous cesarean section: a meta-analysis of observational studies. BMC Pregnancy Childbirth 2021;21:11.

APPENDIX A

Table A1. Key to Grading of Recommendations, Assessment, Development and Evaluation Quality of Evidence

Grade	Definition
Strength of recommendation	
Strong	High level of confidence that the desirable effects outweigh the undesirable effects (strong recommendation for) or the undesirable effects outweigh the desirable effects (strong recommendation against)
Conditional [a]	Desirable effects probably outweigh the undesirable effects (weak recommendation for) or the undesirable effects probably outweigh the desirable effects (weak recommendation against)
Quality of evidence	
High	High level of confidence that the true effect lies close to that of the estimate of the effect
Moderate	Moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect
Very low	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Do not interpret conditional recommendations to mean weak evidence or uncertainty of the recommendation.
Adapted from GRADE Handbook (2013), Table 5.1.

Table A2. Implications of Strong and Conditional recommendations, by guideline user

Perspective	Strong Recommendation • "We recommend that…" • "We recommend to not…"	Conditional (Weak) Recommendation • "We suggest…" • "We suggest to not…"
Authors	The net desirable effects of a course of action outweigh the effects of the alternative course of action.	It is less clear whether the net desirable consequences of a strategy outweigh the alternative strategy.
Patients	Most individuals in the situation would want the recommended course of action, while only a small proportion would not.	The majority of individuals in the situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that patient choices will vary by individual and that clinicians must help patients arrive at a care decision consistent with the patient's values and preferences.
Policymakers	The recommendation can be adapted as policy in most settings.	The recommendation can serve as a starting point for debate with the involvement of many stakeholders.

Adapted from GRADE Handbook (2013), Table 6.1.

APPENDIX B

Misoprostol Solution Preparation

Dissolve 100 μg of misoprostol in 20 mL of warm water or 200 μg of misoprostol in 40 mL of warm water, yielding a concentration of 5 μg/mL of misoprostol. Other concentrations may be used. Label the solution with the concentration.

A large syringe works well to mix, store, and dispense the solution. The solution is stable for 24 hours. Small flakes of the starch carrier may remain undissolved, which does not affect the concentration of active medication.

APPENDIX C

Titrated Oral Misoprostol Solution for Labour Induction: Sample Protocol

1. Ensure the criteria for PGE_1 are met and consent for IOL has been obtained. A 20 minute normal EFM is required prior to starting misoprostol.
2. Prepare and label the solution (see Appendix B).
3. If the cervix is <3 cm dilated, consider a cervical balloon either for 12 hours before starting PGE_1 or concurrently with PGE_1.
4. Start with a 20 μg dose of misoprostol solution.
5. Administer every 2 hours. This dose should be repeated 1−3 times before titrating up.
6. The maximum dose is 50 μg of misoprostol solution.
7. Continuous EFM is required for at least 20 minutes post administration. If there are no signs of active labour after 30 minutes, encourage ambulation until the next dose.
8. When signs of active labour present, establish EFM. Continue ambulation as per the fetal health surveillance guidelines.
9. Artificial rupture of membranes may be performed at any time once the Bishop score is 7 or greater.
10. Once the patient is in active labour, consider IV access.
11. Once active labour begins, the dose should be titrated based on contraction frequency and cervical change. The clinician can choose to increase, maintain, or decrease the next scheduled dose based on EFM and labour progress.
12. If labour is not established within 24 hours (12 doses of q2h misoprostol), consider an alternate method of IOL, or consider postponing induction if it is safe to do so.

APPENDIX D

Misoprostol Solution Sample Protocol Worksheet

Time	Dose[a]	Volume	Signature
08:30	20 μg	4 mL	
10:30	20 μg	4 mL	
12:30	20 μg	4 mL	
14:30	30 μg	6 mL	
16:30	30 μg	6 mL	
18:30	30 μg	6 mL	
20:30	40 μg	8 mL	
22:30	40 μg	8 mL	
00:30	40 μg	8 mL	
02:30	50 μg	10 mL	
04:30	50 μg	10 mL	
06:30	50 μg	10 mL	

[a]Once labour is established, do not increase the dose further. Maintain the current dose or decrease if tachysystole develops.