



HTA

HEALTH TECHNOLOGY INQUIRY SERVICE (HTIS)

**TITLE: Ibuprofen versus Indomethacin for the Closure of Patent Ductus Arteriosus in Neonates: Comparative Effectiveness**

**DATE:** 09 September 2008

**RESEARCH QUESTION:**

What is the comparative effectiveness of ibuprofen versus indomethacin for the closure of patent ductus arteriosus in neonates?

**METHODS:**

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 3, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 2003 and Sept 2008, and are not limited by language. No filters were applied to limit the retrieval by study type.

**RESULTS:**

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials (RCTs) and observational studies.

Four systematic reviews, one meta-analysis, six RCTs, and seven observational studies were identified pertaining to the comparative effectiveness of ibuprofen versus indomethacin for the closure of patent ductus arteriosus in neonates. No relevant health technology assessments were identified. Additional information that may be of use has been included in the Appendix.

**Health technology assessments**

No literature identified.

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**Systematic reviews and meta-analyses**

1. Malviya M, Ohlsson A, Shah S. Surgical versus medical treatment with cyclooxygenase inhibitors for symptomatic patent ductus arteriosus in preterm infants. *Cochrane Database Syst Rev* 2008;(1):CD003951. [PubMed: PM18254035](#)
2. Ohlsson A, Walia R, Shah S. Ibuprofen for the treatment of patent ductus arteriosus in preterm and/or low birth weight infants. *Cochrane Database Syst Rev* 2008;(1):CD003481. [PubMed: PM18254020](#)
3. Aranda JV, Thomas R. Systematic review: intravenous Ibuprofen in preterm newborns. *Semin Perinatol* 2006;30(3):114-20. [PubMed: PM16813969](#)
4. Thomas RL, Parker GC, Van OB, Aranda JV. A meta-analysis of ibuprofen versus indomethacin for closure of patent ductus arteriosus. *Eur J Pediatr* 2005;164(3):135-40. [PubMed: PM15717178](#)
5. Shah SS, Ohlsson A. Ibuprofen for the prevention of patent ductus arteriosus in preterm and/or low birth weight infants. *Cochrane Database Syst Rev* 2003;(2):CD004213. [PubMed: PM12804505](#)

**Randomized controlled trials**

6. Pourarian S, Pishva N, Madani A, Rastegari M. Comparison of oral ibuprofen and indomethacin on closure of patent ductus arteriosus in preterm infants. *East Mediterr Health J* 2008;14(2):360-5. [PubMed: PM18561728](#)
7. Su BH, Lin HC, Chiu HY, Hsieh HY, Chen HH, Tsai YC. Comparison of ibuprofen and indometacin for early-targeted treatment of patent ductus arteriosus in extremely premature infants: a randomised controlled trial. *Arch Dis Child Fetal Neonatal Ed* 2008;93(2):F94-F99. [PubMed: PM17768157](#)
8. Aly H, Lotfy W, Badrawi N, Ghawas M, bdel-Meguid IE, Hammad TA. Oral Ibuprofen and ductus arteriosus in premature infants: a randomized pilot study. *Am J Perinatol* 2007;24(5):267-70. [PubMed: PM17484080](#)
9. Fakhraee SH, Badiee Z, Mojtahedzadeh S, Kazemian M, Kelishadi R. Comparison of oral ibuprofen and indomethacin therapy for patent ductus arteriosus in preterm infants. *Zhongguo Dang Dai Er Ke Za Zhi* 2007;9(5):399-403. [PubMed: PM17937843](#)
10. Chotigeat U, Jirapapa K, Layangkool T. A comparison of oral ibuprofen and intravenous indomethacin for closure of patent ductus arteriosus in preterm infants. *J Med Assoc Thai* 2003;86 Suppl 3:S563-S569. [PubMed: PM14700149](#)
11. Su PH, Chen JY, Su CM, Huang TC, Lee HS. Comparison of ibuprofen and indomethacin therapy for patent ductus arteriosus in preterm infants. *Pediatr Int* 2003;45(6):665-70. [PubMed: PM14651538](#)

## Observational studies

12. Erdeve O, Sarici SU, Sari E, Gok F. Oral-ibuprofen-induced acute renal failure in a preterm infant. *Pediatr Nephrol* 2008;23(9):1565-7. [PubMed: PM18446376](#)
13. Cherif A, Jabnoun S, Khrouf N. Oral ibuprofen in early curative closure of patent ductus arteriosus in very premature infants. *Am J Perinatol* 2007;24(6):339-45. [PubMed: PM17564958](#)
14. Desfrere L, Zohar S, Morville P, Brunhes A, Chevret S, Pons G, et al. Dose-finding study of ibuprofen in patent ductus arteriosus using the continual reassessment method. *J Clin Pharm Ther* 2005;30(2):121-32. [PubMed: PM15811164](#)
15. Fanos V, Benini D, Verlato G, Errico G, Cuzzolin L. Efficacy and renal tolerability of ibuprofen vs. indomethacin in preterm infants with patent ductus arteriosus. *Fundam Clin Pharmacol* 2005;19(2):187-93. [PubMed: PM15810899](#)
16. Tatli MM, Kumral A, Duman N, Demir K, Gurcu O, Ozkan H. Spontaneous intestinal perforation after oral ibuprofen treatment of patent ductus arteriosus in two very-low-birthweight infants. *Acta Paediatr* 2004;93(7):999-1001. [PubMed: PM15303820](#)
17. Heyman E, Morag I, Batash D, Keidar R, Baram S, Berkovitch M. Closure of patent ductus arteriosus with oral ibuprofen suspension in premature newborns: a pilot study. *Pediatrics* 2003;112(5):e354. [PubMed: PM14595076](#)
18. Sharma PK, Garg SK, Narang A. Pharmacokinetics of oral ibuprofen in premature infants. *J Clin Pharmacol* 2003;43(9):968-73. [PubMed: PM12971028](#)

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**APPENDIX – FURTHER INFORMATION:****Systematic reviews and meta-analyses- prophylaxis for PDA**

19. Shah SS, Ohlsson A. Ibuprofen for the prevention of patent ductus arteriosus in preterm and/or low birth weight infants. *Cochrane Database Syst Rev* 2006;(1):CD004213. [PubMed: PM16437478](#)

**Randomized controlled trials- prophylaxis for PDA**

20. Sangtawesin V, Sangtawesin C, Raksasinborisut C, Sathirakul K, Kanjanapattanakul W, Khorana M, et al. Oral ibuprofen prophylaxis for symptomatic patent ductus arteriosus of prematurity. *J Med Assoc Thai* 2006;89(3):314-21. [PubMed: PM16696414](#)

**Review articles**

21. Sekar KC, Corff KE. Treatment of patent ductus arteriosus: indomethacin or ibuprofen? *J Perinatol* 2008;28 Suppl 1:S60-S62. [PubMed: PM18446180](#)
22. Donze A, Smith JR, Bryowsky K. Safety and efficacy of ibuprofen versus indomethacin for the treatment of patent ductus arteriosus in the preterm infant: reviewing the evidence. *Neonatal Netw* 2007;26(3):187-95. [PubMed: PM17521065](#)
23. Giniger RP, Buffat C, Millet V, Simeoni U. Renal effects of ibuprofen for the treatment of patent ductus arteriosus in premature infants. *J Matern Fetal Neonatal Med* 2007;20(4):275-83. [PubMed: PM17437233](#)
24. Poon G. Ibuprofen lysine (NeoProfen) for the treatment of patent ductus arteriosus. *Proc (Bayl Univ Med Cent)* 2007;20(1):83-5. [PubMed: PM17256050](#)
25. Teixeira LS, McNamara PJ. Enhanced intensive care for the neonatal ductus arteriosus. *Acta Paediatr* 2006;95(4):394-403. [PubMed: PM16720484](#)
26. Flores M. Ibuprofen: alternative treatment for patent ductus arteriosus. *Neonatal Netw* 2003;22(2):27-31. [PubMed: PM12696723](#)

**Additional references**

27. Swartz EN. Is indomethacin or ibuprofen better for medical closure of the patent ductus arteriosus? *Arch Dis Child* 2003;88(12):1134-5. [PubMed: PM14670792](#)