Chlorhexidine

Essential medicine status ✓

EMLc | ATC codes: D08AC02

Indication	Omphalitis of newborn ICD11 code: KA65.1
INN	Chlorhexidine
Medicine type	Chemical agent
List type	Core
Additional notes	For umbilical cord care
Formulations	**Local > Topical > Solution:** 7.1% chlorhexidine digluconate (delivering 4% chlorhexidine) (EMLc) **Local > Topical > Gel:** 7.1% chlorhexidine digluconate (delivering 4% chlorhexidine) (EMLc)
EML status history	First added in 2013 (TRS 985)
Sex	All
Age	Newborn (< 1 month)
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Chlorhexidine
DrugBank	Chlorhexidine

Summary of evidence and Expert Committee recommendations

The application to include chlorhexidine digluconate 7.1% solution or gel delivering 4% chlorhexidine for cord care was submitted by the Program for Appropriate Technology in Health (PATH), Chlorhexidine Working Group. In 2009, the Expert Committee reviewed an application to include this formulation of chlorhexidine. Although there was general consensus that, in unclean deliveries, topical antiseptics may help in reducing infections, there was no clear evidence regarding the superiority of any one product. In addition, no product was commercially available at that time. A 20% solution was added for dilution. In 2011 an updated application was submitted to replace the 20% listing with a ready-made 7.1% digluconate solution or gel. At that time, trials were continuing and the product was still not commercially available. The Committee then decided to list 4% chlorhexidine as one of the missing priority products in the “Priority medicines for mothers and children – 2011”. An updated application was submitted to the 19th meeting of the Expert Committee for inclusion of the 7.1% concentration providing 4% free chlorhexidine formulation. It was felt that there is a need to specify concentrations correctly: 20.0% chlorhexidine digluconate provides 11.3% free chlorhexidine, while 7.1% provides 4.0%, and 5.0% provides 2.8%. The evidence in the application consisted of three trials conducted in community settings in Bangladesh, Nepal and Pakistan where there were high rates of home deliveries and high neonatal mortality (1-3). Over 50 000 newborns were enrolled, and the trial compared single or multiple applications of chlorhexidine with standard dry cord care practices. The results showed significant reductions in neonatal mortality (24%) and omphalitis (75%). Systematically collected data on long- and short-term adverse events are scant. However, chlorhexidine was used widely in randomized trials and has been used elsewhere for neonates (4, 5). Transient contact dermatitis has been reported in preterm very-low-birth-weight infants after long-term (> 7 days) placement of chlorhexidine-impregnated dressings for central venous catheters (4). Although a significant effect was seen for neonatal mortality and omphalitis, the studies were predominantly in high-mortality home birth settings in South Asia. The findings are therefore difficult to generalize to settings where the majority of births take place in health facilities and where neonatal mortality rates are lower. Questions remain about the optimal treatment regimen with respect to timing of the application of chlorhexidine, as well as the number of applications. Compared with dry and clean care (mean 4.78 days), separation time of

the umbilical cord was longer in the single (mean 6.90 days, difference = 2.10, 95% CI: 1.85–2.35) and multiple (mean 7.49 days, difference = 2.69, 95% CI: 2.44–2.95) cleansing groups in a cluster randomized trial (6). This outcome may affect carer satisfaction, but the clinical importance is unclear. The scalability and integration of the use of chlorhexidine into existing health systems have yet to be established. Two of the three studies that showed beneficial effects of chlorhexidine application to the cord included several visits by health-care workers, which may not be possible in all settings. There is now a commercially available product in at least Bangladesh and India but there is as yet no global supply. Local production of the product may be an appropriate strategy to ensure adequate supply, although the precise concentration required in the formulation means that standards for the manufacturing process need to be ensured. The Expert Committee recommended the listing of the new 4% gel formulation, the deletion of the 20% solution, and the retention of the 5% solution. The Committee hoped that inclusion in the list would increase the chances of making a commercial product available and noted that three manufacturers (two in India and one in Belgium) are already providing the gel product. References 1. Arifeen SE, Mullany LC, Shah R, Mannan I, Rahman SM, Talukder MR, et al. The effect of cord cleansing with chlorhexidine on neonatal mortality in rural Bangladesh: a communitybased, cluster-randomised trial. Lancet. 2012;379(9820):1022-8. http://dx.doi.org/10.1016/S0140- 6736(11)61848-5 PMID:22322124 2. Soofi S, Cousens S, Imdad A, Bhutto N, Ali N, Bhutta ZA. Topical application of chlorhexidine to neonatal umbilical cords for prevention of omphalitis and neonatal mortality in a rural district of Pakistan: a community-based, cluster-randomised trial. Lancet. 2012;379(9820):1029-36. http:// dx.doi.org/10.1016/S0140-6736(11)61877-1 PMID:22322126 3. Mullany LC, Darmstadt GL, Khatry SK, Katz J, LeClerq SC, Shrestha S, et al. Topical applications of chlorhexidine to the umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: a community-based, cluster-randomised trial. Lancet. 2006;367(9514):910-8. http://dx.doi.org/10.1016/S0140-6736(06)68381-5 PMID:16546539 4. Garland JS, Alex CP, Mueller CD, Otten D, Shivpuri C, Harris MC, et al. A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. Pediatrics. 2001;107(6):1431-6. http://dx.doi.org/10.1542/ peds.107.6.1431 PMID:11389271 5. Tamma PD, Aucott SW, Milstone AM. Chlorhexidine use in the neonatal intensive care unit: results from a national survey. Infect Control Hosp Epidemiol. 2010;31(8):846-9. http://dx.doi.org/10.1086/655017 PMID:20586654 6. Mullany LC, Shah R, El Arifeen S, Mannan I, Winch PJ, Hill A, et al. Chlorhexidine cleansing of the umbilical cord and separation time: a cluster-randomized trial. Pediatrics. 2013;131(4):708-15. http://dx.doi.org/10.1542/peds.2012-2951 PMID:23509175