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SPECIAL ARTICLE

Assessing the global availability of misoprostol

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ABSTRACT

Objective: To assess the worldwide availability of misoprostol. Documenting the extent of misoprostol use in obstetrics-gynecology is difficult because the drug typically is unregistered for such indications. **Methods:** Data for 2002–2007 on annual sales (measured in weight) to hospitals and retail pharmacies, plus manufacturer prices per 200- μ g misoprostol, were analyzed for medications containing misoprostol alone or combined with a nonsteroidal anti-inflammatory drug (NSAID); regional and country-specific trends were identified. Consumer prices per pill are documented for all formulations of registered medications. **Results:** Of the misoprostol sold worldwide, 70% was misoprostol-NSAID-combination drugs; of this, 91% was sold in North America and Western Europe. Asia sold the most misoprostol-only drugs; sales increased dramatically in Bangladesh (by 128%) and India (646%), where various low-price brands are sold. Misoprostol sales decreased in Latin America but increased in the Middle East-North Africa and Sub-Saharan Africa; these regions generally had low amounts sold per population. **Conclusion:** Availability is improving in some low-income regions where misoprostol could significantly reduce maternal deaths due to postpartum hemorrhage and unsafe abortion.

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1. Introduction

Misoprostol, a synthetic prostaglandin E₁ analogue, is approved in more than 80 countries for the prevention and treatment of gastric ulcers caused by long-term nonsteroidal anti-inflammatory drug (NSAID) use. A burgeoning literature and experience also support its use in obstetrics-gynecology [1–3]. Effective in labor induction, the treatment of incomplete or missed abortion, the prevention and treatment of postpartum hemorrhage (PPH), and the elective termination of pregnancy, misoprostol is considered potentially lifesaving, particularly in low-resource settings [4–6].

In the United States, most of Western Europe, and several Asian and African countries, misoprostol is part of the approved regimen for inducing abortion; the World Health Organization recommends mifepristone combined with misoprostol as the most effective method of medical abortion [7]. Where mifepristone is unavailable, however, misoprostol alone is being used by providers to terminate unwanted pregnancies and by women to self-induce abortion [8]. Particularly important is the use of misoprostol to prevent PPH, the leading cause of maternal mortality worldwide [9]. In some low-resource settings where other uterotonics are unavailable or cannot be properly stored, or where the skilled attendants needed for intravenous or intramuscular administration are in short supply, misoprostol—a fairly inexpensive, heat-stable drug that can be self-administered—is used to effectively treat and

prevent PPH [5,8]. Researchers recently found that making misoprostol readily available in low-resource areas for use in termination of pregnancy and management of PPH would do more than any other realistically achievable, sustainable, large-scale intervention to save the lives of women at risk for death by maternal causes [10].

Although misoprostol's benefits in obstetrics-gynecology are well-established [1–3] and the drug's potential to significantly reduce maternal mortality in low-income countries is clear [5,8,10], in most places misoprostol is available for reproductive health care through off-label use only. Relatively few countries have misoprostol brands registered for obstetric-gynecologic indications (Table 1). Although many medications are used off-label [11], this status for misoprostol severely limits its application and complicates efforts to document its use.

We analyzed sales of all misoprostol-containing drugs sold in a recent 6-year period, identifying trends by region and country. The goals were to assess the availability of misoprostol in high- and low-resource regions and to roughly gauge the amount of misoprostol drug-use for obstetric-gynecologic indications. In assessing the drugs' availability and uses in various regions, we consider pertinent demographic, historical, and legal factors that help explain the observed trends and identify areas of unmet need. Monitoring the availability of misoprostol is an important step toward ensuring continued access to the drug.

2. Methods

Ipas purchased sales data for 2002–2007 on all misoprostol medications from IMS Health (Norwalk, CT, USA). We report annual

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Table 1

Examples of countries with proprietary misoprostol drugs licensed for reproductive health indications.

Country	Brand (Manufacturer)	Approved Ob-Gyn indication
Brazil, Peru	Prostokos (Hebron, Caruaru PE, Brazil)	Labor induction, uterine evacuation after fetal death, legal termination of pregnancy
Egypt	Vagiprost (Adwia, El Oubor, Egypt)	Labor induction
France	Gymiso (HRA Pharma, Paris, France)	Legal termination of pregnancy
Russia	Mirolut (Mir-Pharm, Moscow, Russia)	Termination of pregnancy in combination with mifepristone
	Mizoprostol (Beijing Zizhu Pharmaceutical Co., Beijing, China), Beijing, China)	Termination of pregnancy in combination with mifepristone, treatment of PPH
Spain	Misive/Bial (Madrid, Spain)	Medical termination of pregnancy (with or without mifepristone)
	Misofar/Bial (Madrid, Spain)	Dilatation of cervix, treatment of incomplete or missed spontaneous abortion or after intrauterine fetal death.
India	Cytolog (Zydus Cadila, Gujarat, India)	Induction of labor, cervical ripening, termination of pregnancy
	Medabon (Sun Pharma, Mumbai, India)	Medical Termination of pregnancy up to 63 days gestation
	Misoprost (Cipla Pharmaceuticals, Mumbai, India)	Cervical ripening, termination of pregnancy, prevention and treatment of PPH
	Prestakind (Mankind, New Delhi, India)	Induction of labor, cervical ripening, termination of pregnancy
	Zitotec (Sun Pharma, Mumbai, India)	Induction of labor, cervical ripening, termination of pregnancy, prevention and treatment of PPH
Nepal	Isovent (Square Pharmaceuticals, Dhaka, Bangladesh)	Termination of pregnancy, prevention and treatment of PPH
	Misoprost (Cipla Pharmaceuticals, Mumbai, India)	Termination of pregnancy
	Zitotec (Sun Pharma, Mumbai, India)	Termination of pregnancy, prevention and treatment of PPH
Bangladesh	GMisoprostol (Gonoshasthaya Pharmaceuticals, Dhaka, Bangladesh)	Labor induction, prevention and treatment of PPH
	Isovent (Square Pharmaceuticals, Dhaka, Bangladesh)	Labor induction, prevention and treatment of PPH
Ghana	Misotac (Sigma Pharmaceutical Industries, Menofya, Egypt)	Prevention and treatment of PPH
Kenya	Isovent (Square Pharmaceuticals, Dhaka, Bangladesh)	Cervical ripening, missed or incomplete abortion, prevention and treatment of PPH
Nigeria	Mizoprostol (Beijing Zizhu Pharmaceutical Co., Beijing, China), Beijing, China)	Prevention and treatment of PPH
Sudan	Misotac (Sigma Pharmaceutical Industries, Menofya, Egypt)	Prevention and treatment of PPH
Tanzania	Misotac (Sigma Pharmaceutical Industries, Menofya, Egypt)	Prevention and treatment of PPH
Uganda	Misotac (Sigma Pharmaceutical Industries, Menofya, Egypt)	Prevention and treatment of PPH
Zambia	Misotac (S Sigma Pharmaceutical Industries, Menofya, Egypt)	Prevention and treatment of PPH
	Mizoprostol (Beijing Zizhu Pharmaceutical Co., Beijing, China)	Termination of pregnancy in combination with mifepristone

Notes:

In several other countries, including the United States, misoprostol is approved for obstetric indications, but no dedicated brand is registered in the country for that purpose.

PPH stands for postpartum hemorrhage. Medabon combines 1 tab of mifepristone 200 mg and 4 tabs of misoprostol 200 µg. Some of the brands listed above may carry additional indications.

Table 2

Total amount (weight) of misoprostol sold annually, by region and country, according to drug type^a.

Region and country ^d	Misoprostol-only drugs			Misoprostol-NSAID drugs		
	Sales in 2007 (µg × 10 ⁶)	% change 2002–2007	µg/population in 2007	Sales in 2007 (µg × 10 ⁶)	% change 2002–2007	µg/population in 2007
GLOBAL (TOTAL)	39 051.0	–15	3.7	90 249.0	–4	8.6
NORTH AMERICA	6489.5	–29	23.6	30 580.1	–1	91.6
United States	5523.2	–20	18.5	16 806.5	–23	56.3
Canada	951.6	–57	28.8	13 688.9	49	413.6
Puerto Rico	14.7	–47	3.8	84.7	1	21.6
WESTERN EUROPE	6020.6	–55	15.2	51 159.1	–14	128.9
United Kingdom	536.6	–39	8.9	16 780.7	–9	276.9
France	1848.5	–39	29.5	7782.3	–4	124.0
Spain	427.1	–47	10.6	8386.5	–28	207.6
Germany	149.0	–74	1.8	4490.4	–34	54.5
Netherlands	38.3	–55	2.3	4653.9	3	282.2
Italy	2458.9	–67	42.3	1829.6	–33	31.5
Sweden	121.2	–42	13.4	1237.8	–23	137.3
Denmark	24.0	14	4.4	989.8	38	181.6
Switzerland	56.6	–5	7.5	897.6	8	119.3
Austria	25.8	–64	3.2	1184.2	30	144.6
Portugal ^e	121.8	–37	11.5	1112.1	–5	104.9
Norway	40.0	38	8.7	784.9	11	170.2
Ireland ^e	16.7	–19	4.1	755.2	52	185.9
Finland	37.3	–8	7.1	204.6	–53	39.1
Luxembourg ^e	2.6	4	5.5	39.7	–32	83.6
Belgium	29.8	69	2.9	29.6	–21	2.9
Greece ^e	86.3	33	8.1	0.2	–95	0.0
EASTERN EUROPE	22.7	–53	0.1	760.2	55	3.3
Romania	– ^b	–	– ^b	103.5	70	4.6
Estonia	0.1	–87 ^c	0.1	11.9	–64	9.0
Slovenia	0.3	18 ^c	0.2	– ^b	–	– ^b
Lithuania	2.5	62	0.7	– ^b	–	– ^b
Latvia	0.1	–69	0.1	0.0	–100	0.0
Czech Republic	0.0	–94	0.0	– ^b	–	– ^b
Slovakia	– ^b	–	– ^b	572.9	160	105.3
Poland	13.0	–17	0.3	71.6	–30	1.9
Russia	6.6	–78	0.1	0.3	–100	0.0
ASIA	21 524.3	7	6.4	4820.6	216	1.4
Japan	10 450.0	–3	82.0	– ^b	–	– ^b
India	5494.5	646	5.0	288.8	268 ^c	0.3
South Korea	3388.2	–27	69.4	– ^b	–	– ^b
Pakistan ^e	– ^b	–	– ^b	2531.1	254	15.3
Indonesia	223.9	116	0.9	– ^b	–	– ^b
China ^f	1343.4	67	1.0	0.6	–	– ^b
Bangladesh ^e	257.2	128	1.8	1911.3	817 ^c	13.0
Malaysia	89.5	0	3.7	– ^b	–	– ^b
Australia	87.0	–47	4.3	40.7	–43	2.0
Hong Kong	46.2	–54	6.7	4.1	–94	0.6
Taiwan	32.3	–58	1.4	44.1	–66	1.9
Thailand ^f	62.8	–42	1.0	– ^b	–	– ^b
New Zealand	35.9	–90	8.8	– ^b	–	– ^b
Singapore	13.6	5	3.0	– ^b	–	– ^b
Philippines	– ^b	–	– ^b	– ^b	–	– ^b
LATIN AMERICA	2637.3	–17	5.1	1053.3	–30	2.1
Mexico ^e	1157.2	–13	10.8	554.7	–31	5.2
Argentina ^e	– ^b	–	– ^b	362.5	–34	9.1
Venezuela ^e	773.5	26	30.1	105.5	–3	4.1
Central America ^e	147.4	16	3.8	– ^b	–	– ^b
Colombia ^e	92.3	–87	2.1	– ^b	–	– ^b
Ecuador ^e	251.5	25	18.6	20.4	1605 ^c	1.5
Dominican Republic ^e	137.6	–10	15.0	10.1	–37	1.1
Uruguay ^e	11.2	261	3.3	– ^b	–	– ^b
Chile ^e	21.6	–2	1.3	– ^b	–	– ^b
Peru ^e	44.8	–10	1.6	– ^b	–	– ^b
Brazil ^e	0.3	16 ^c	0.0	– ^b	–	– ^b
SUB-SAHARAN AFRICA	477.2	27	3.0	870.2	–9	5.5
South Africa	364.8	30	8.3	870.2	–9	19.7

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