

International Consortium for Medical Abortion
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Product issues in medical abortion

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Product issues in medical abortion

- Products
- Patents
- Availability and cost of drugs
- Drug approval
- Impact of WTO TRIPS

Products and patents

- Three medical abortion regimens in use:
 - Misoprostol-only
 - Methotrexate-misoprostol combination
 - Mifepristone-misoprostol combination
- All three drugs are off patent worldwide.
 - US patent for mifepristone + PG (Schering) expired last week - 12 Oct 04 (Danco market exclusivity continues until 28 Sept 05).

Product availability

- Misoprostol and methotrexate are widely available very cheaply in many countries.
- Searle (part of Pfizer), registered misoprostol (as Cytotec) worldwide, except for Africa (other than South Africa or Ghana), India, most of the Middle East and central Asia, for the prevention of gastric ulcers associated with the use of nonsteroidal anti-inflammatory drugs.
- Misoprostol also available as generic preparations.

Product availability

- Misoprostol widely used off-label with mifepristone for medical abortion. USFDA and other DRAs, acknowledge use for medical abortion.
- Mifepristone has limited availability – is approved and sold in 29 countries.
- Mifepristone is the most expensive of these drugs because of relatively complex synthesis - small-scale and low yield; and small sales volume worldwide.

Mifepristone - availability

- Many countries are in the developed world:
12 EU countries (all pre-1 May 04 countries – except Ireland, Italy and Portugal), New Zealand, Norway, Switzerland, USA.
- Developing countries and countries in transition:
Azerbaijan, China, Georgia, India, Israel, Moldova, Russian Federation, South Africa, Taiwan, Tunisia, Ukraine, Uzbekistan, Viet Nam.

Mifepristone - history

- Roussel-Uclaf synthesized and patented RU-486 (mifepristone) in 1980.
- In 1983, Karolinska Institute/WHO showed increased efficacy when used with a PG (patented by Schering!).
- Roussel-Uclaf began commercialization in western Europe.
- After takeover by Hoechst AG, product was divested from portfolio and patent and product rights given to a small, single product French company, Exelgyn.

Mifepristone - history

- In 1986, were uncompleted license negotiations between Roussel-Uclaf and China. Chinese SFPC commissioned synthesis and subsequent clinical trial of mifepristone.
- In 1993, Roussel-Uclaf donated rights for the USA to the Population Council.
- The Population Council licensed Danco as the commercial entity to bring Mifeprex to the US market, using bulk mifepristone from China.

Mifepristone - manufacture

- Few other commercial manufacturers are producing mifepristone API. These include:
 - China (3); India (1 out of 3 companies);
 - Taiwan (2)
- Chinese manufacturers deliver bulk product for tableting in other countries:
 - India (2); Vietnam (1); US (1)

Retail price

Mifepristone, 600mg

- USA: \$250
- South Africa: \$220
- Germany, Switzerland :\$130-140
- UK: \$75 (only available in hospitals and other licensed facilities)
- China, India, Viet Nam: \$6-8.

Retail price

United Kingdom

- Misoprostol: 140 tabs 200µg £23.40
1 tab 200µg \$0.30
- Mifepristone: 3 tabs 200mg £41.83
1 tab 200mg \$25

South Africa

- Misoprostol: 120 tabs 200µg Rand415.60
1 tab 200µg \$0.50
- Mifepristone: 3 tabs 200mg Rand1448.00
1 tab 200mg \$73

Mifepristone - availability

- Most of these countries represent the best opportunity markets for a drug, because of:
 - highest possible market prices (developed world)
 - ease of registration (lowest possible opportunity costs)
 - high market volume (highest possible opportunity rewards)
- Markets that do not meet these conditions are not likely to be commercially attractive for product introduction since opportunity costs are not offset by commercial rewards.

Mifepristone - pricing

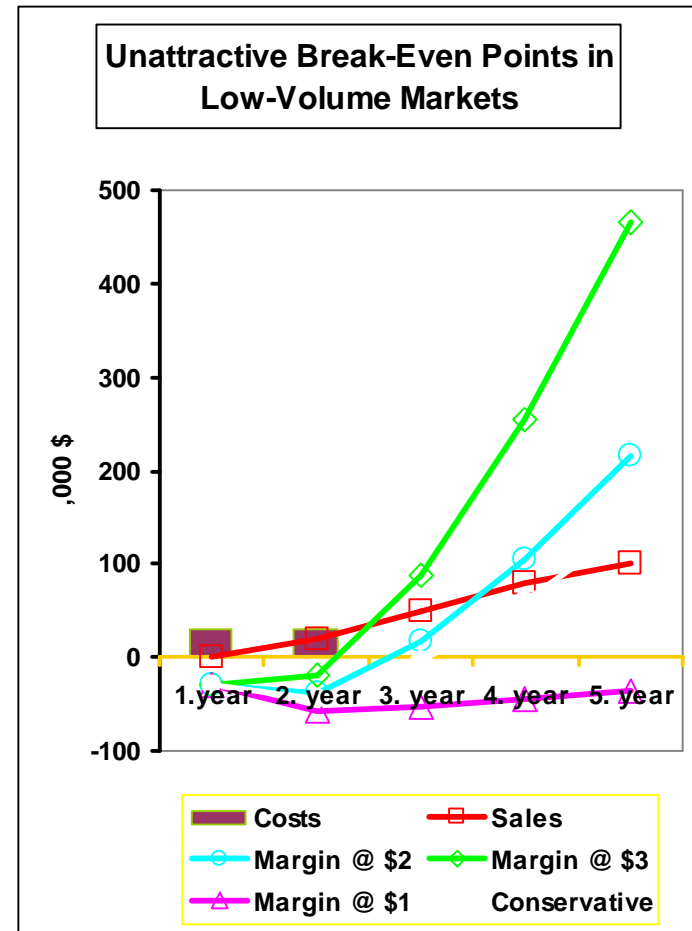
- Exelgyn and Danco serve the wealthy countries worldwide at highest possible market prices.
- Entry into these markets for developing country manufacturers come with very high opportunity costs. (FDA regulations, drug approval)
- Developing country manufacturers serve their own markets where:
 - Opportunity costs are lowest (China, India, Taiwan, Viet Nam).
 - High opportunity rewards and large potential markets exist (China, India, Ukraine, Viet Nam).
 - Ease of registration (China, India, Taiwan, Ukraine, Viet Nam).
- BUT – when these situations do not exist and where product prices must be LOW, it's a different story:

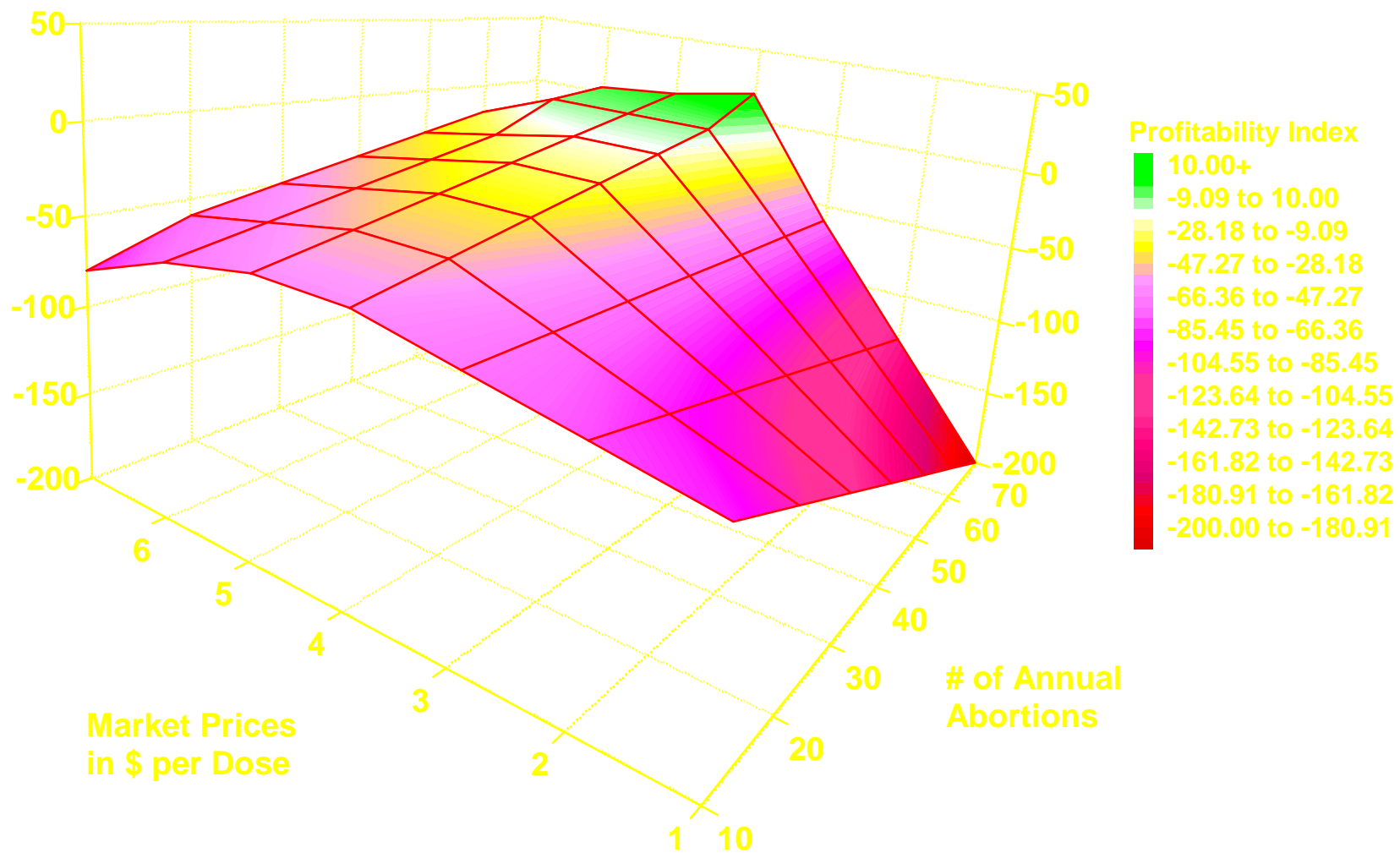
Pricing scenario

- Given estimated costs of \$50k - \$80k for product introduction into a developing country market, volumes and prices have to be commercially significant to justify product launch.

(Example: 100,000 medical abortions annually; product costs @ \$.90; sales prices @ \$1, \$2, \$3; Conservative case: 50,000 medical abortions annually @ \$2.50)

- Reality check demonstrates low commercial incentives for product introduction.





Mifepristone pricing

- There are limited commercial incentives to sell into other markets.
- Preferred locations for product launch are territories with:
 - low opportunity costs; ease of registration;
 - high opportunity rewards (either large markets
 - or higher prices; preferably both!).
- Mifepristone as a drug is not a commercial success story. This limits its availability!

Annual number of medical abortions

Impossible to estimate

- Total number of legal abortions: 26+ million?
- China: 10+ million? How many are med abortion?
- India: 6 million? But only 723,000 legal cases reported (2001) – MF/MS unrestricted
- Viet Nam: 1,530,000 (2000), med ab low
- USA: 1,310,000 (2000); 230,000 by PPFA (25% med abortion)
- England & Wales, 181,600 (2002) - 14% med abortion; Scotland, 11,600 (2002) - 50% med abortion.
- Are there 1,000,000 or 10,000,000? Probably only c. 250,000 outside China and India.

Mifepristone – availability and pricing

- Mifepristone availability will expand and price decrease if development of other clinical indications open a larger patient pool as commercial target beyond medical abortion.
- Are 126 patents for other uses, from cancer to contraception, fibroids to Cushing's syndrome.
- But these clinical indications need to provide large mainstream, not small niche, markets, otherwise required market size will not be achieved.

Drug registration

- The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has developed the ICH Common Technical Document to provide common product registration requirements.
- It is beginning to be applied in the USA, the European Union and Japan (which make up almost 75% of the global pharmaceutical market)
and is intended to be used worldwide.

Drug registration

- Drug registration in all countries needs to follow a NDA format - both time consuming and costly, if commercial return not likely. In some countries, locally produced clinical trial data may be required.
- Generic registration likely to be possible only in the 29 countries where registration already exists.

WTO agreement on trade-related aspects of intellectual property (TRIPS)

- TRIPS establishes minimum standards for protecting and enforcing IP rights. Major generic drug producing countries like India and China must adhere to TRIPS from 2005 and the least developed countries from 2016. Countries with insufficient manufacturing know how or capacity can use compulsory licences to import generic products from producer countries BUT only in emergencies.
- Does not apply for use of current drugs for medical abortion since products off patent nor will they qualify under emergency situations. Would be applicable if IP is created for new uses of mifepristone.

Registration of Mifepristone

- *How can we make mifepristone more*
- *widely available at reasonable cost both in*
- *countries where it is registered and in others?*
- *How can we ensure appropriate quality of care*
- *in those countries it is available?*