Evening Primrose Oil Safety during Pregnancy and Breast Feeding

A) CLINICAL TOXICOLOGY

These literature searches to obtain safety information about evening primrose oil were completed on Public Medline using URL http://www.ncbi.nlm.nih.gov/.

Search Number	1	2	3	4
Type & Level of Search	Any	Any	Any	Any
Date of Search	December 18, 2003	December 18, 2003	June 10, 2004	June 11, 2004
Keywords	Evening Primrose Oil and Safety	Evening Primrose Oil and Toxicity	Evening primrose oil and Safety and Pregnancy	Evening primrose oil and breast feeding
Limits	None	None	None	None
Number of Results	10	11	2	4
Number of Relevant Results	0	0	0	0

Evening Primrose Oil
No formal clinical toxicology trials completed in pregnancy or while breast feeding were identified in the literature searched cited in A) above for evening primrose oil. These searches were repeated on July 23, 2007 and did not identify any additional relevant studies. However, there have been some clinical studies that supplemented evening primrose oil during pregnancy and breast feeding that may provide some safety information as follows:

Cant A, Shay J, Horrobin DF. The effect of maternal supplementation with linoleic and γ-linolenic acids on the fat composition and content of human milk: A placebo-controlled trial. *J Nutr Sci Vitaminol*1991;37:573-579.

D'Almeida A, Carter JP, Anatol A, Prost C. Effects of a combination of evening primrose oil (gamma-linolenic acid) and fish oil (eicosapentaenoic acid + docosahexaenoic acid) versus magnesium, and versus placebo in preventing pre-eclampsia. *Women & Health* 1992;19(2/3):117-131.

Dove D. and Johnson P. Oral evening primrose oil: Its effects on length of pregnancy and selected intrapartum outcomes in low-risk nulliparous women. *Journal of Mid-wifery* 1999;44(3):320-324.

Gallager, S. Essential Fatty Acids: Their Role in Pregnancy and Labour. *Pre & Post Natal News.* Summer 2000:2-7.

The relevant information obtained from these studies is as follows:

D'Almeida et al. 1992 - The evening primrose oil/fish oil group had a greater incidence of vomiting than the other two groups. NOTE: It was not possible to determine if these reported side effects were the result of evening primrose oil or fish oil consumption. Given that the symptoms reported are similar to those identified for fish oil consumption and no other studies using evening primrose oil reported similar side effects, one is inclined to conclude that these side effects were the result of fish oil consumption and not due to the evening primrose oil.

Dove and Johnson 1999 – Reported a trend for evening primrose oil treated patients to have more protracted active phase, prolonged rupture of membranes, oxytocin augmentation and arrest of descent. However, it was also noted that the evening primrose oil group had larger babies than the control group.

The dosage of evening primrose oil was 1500 mg/day throughout pregnancy and up to the 37th week of gestation, then 500 mg/day until labor ensued. The dose of evening primrose oil up to the 37th week was approximately three times what would be provided in a daily dose of Efanatal.

Gallager 2000 - A very small percentage of women report a skin rash or more active Braxton-Hicks contractions with evening primrose oil supplementation that can be remedied by reducing the dose. The quantity of evening primrose oil provided in Efanatal is only 540.4 mg and the dosage of evening primrose oil that Gallagher indicated was being used in her patients was 4 g per day. Therefore, the quantity of evening primrose oil in Efanatal is unlikely to produce the side effects mentioned.

Gallager also provided some additional observations that she applied to "essential fatty acid supplementation" in general. These could be contributed to either evening primrose oil, or fish oil, or both and so should be taken into consideration as they relate to Efanatal use. Those observations are as follows:

- EFA intake throughout the pregnancy halves the length of active labour.
- Lacerations and length of early labour also appear to be reduced.
- Women with a history of post-partum hemorrhage should proceed with caution with regard to EFA supplementation. Supplementation for patients on blood thinners should be under medical care.
- EFA intake throughout pregnancy promotes a faster active stage of labour, reduced stretch marks and reduced perineal lacerations.

B. PREVIOUS MARKETING EXPERIENCE

Efanatal has been distributed in a number of countries including Canada for several years. Unfortunately, maintaining adverse reaction reports is not a requirement for this product in countries outside of Canada. Therefore, the only available information is that which was collected within Canada. The following is a summary of capsule/dosage sales and the number of adverse reactions reported for 2001, 2002, 2003 and 2004 (up until June 30th).

Year	2001	2002	2003	2004 (until June 30th)
# of Capsules Sold	204,480	245,580	277,380	117,780
# of Maximum Daily Doses	102,240	122,790	138,690	58,890
# of Adverse Reactions	0	0	0	0

There were no reported adverse reactions during the time interval described above.