



*This information has been gathered by The Cleft Lip & Palate Foundation of Smiles. We are responding to the fact that a number of our members have questions concerning the safety of medications that they had taken during pregnancy, or may take during a future pregnancy. These medications may be the cause of craniofacial differences. Our goal is to ensure that our families have resources and facts about the medications that may be taken during pregnancy, so you can have informed discussions with the treating doctors.*

Online at [www.cleftsmile.org](http://www.cleftsmile.org)

[Join the CleftSmile.org online community](#)

Contact us by email at [rachel@cleftsmile.org](mailto:rachel@cleftsmile.org)

The Cleft Lip & Palate Foundation of Smiles provides research on craniofacial causes (genetics, environmental, prescription drugs), treatments (cleft palate teams, medical devices, therapies), and available support for families.

*This PDF is about Clomid birth defect risks for women who get pregnant while taking this type of pain medication.*



## RESEARCH AND RECENT STUDIES

# Clomid

While fertility drugs can assist in the miracle of birth, they also have side effects for the patient and potential birth defect risks for the baby. Here are some questions and answers to consider.

### What is Clomid?

Clomid is an orally administered non-steroidal fertility treatment used to induce ovulation in women who have difficulty conceiving. Clomid is the brand made by Sanofi Aventis. Synonyms include *clomifene* and *clomiphene citrate*. Serophene is another brand name.

### What is the pharmacodynamics of Clomid?

Clomid is an orally administered, non-steroidal, ovulatory stimulant that acts as a selective estrogen receptor modulator. Its usage can lead to multiple ovulations and increases the risk of multiple births. There may be an increased risk of ovarian cancer and weight gain.

### Have there been any studies with Clomid and birth defects?

There was a Center for Disease Control and Prevention study for the use of clomiphene citrate and birth defects called the National Birth Defects Prevention Study, 1997–2005. Clomiphene citrate (CC) is the first line drug for subfertility treatment. Studies assessing the association between CC and birth defects have been inconclusive.

Data was used from the National Birth Defects Prevention Study, a population-based, multi-site case-control study of major birth defects. Women from ten US regions with deliveries affected by at least one of >30 birth defects (cases) and mothers of live born infants without a major birth defect (controls) who delivered October 1997–December 2005 were interviewed. The exposure of interest was reported in clomiphene citrate use in the period from two months before conception through the first month of pregnancy. Women who conceived using assisted reproductive technology were excluded. Thirty-six birth defect categories with at least three exposed cases were studied.



In conclusion, several associations between clomiphene citrate use and birth defects were observed. However, because of the small number of cases, inconsistency of some findings with previous reports, associations should be interpreted cautiously.

### What are Clomid side effects?

Enlarged ovaries, hot flashes, and abdominal or pelvic pain are some of the most common side effects seen with Clomid. Side effects that are less common and occur in less than 1% of patients may include constipation, diarrhea, and fatigue. Although most Clomid side effects are considered minor, certain side effects should be reported to your healthcare provider immediately, including signs of an allergic reaction, changes in vision, or severe abdominal pain.

### Who should not take Clomid?

You should not take Clomid if you have:

- Thyroid or adrenal problems
- A brain tumor
- Ovarian cysts
- Polycystic ovarian syndrome (PCOS)
- Fibroids
- Depression
- Liver disease, including liver failure
- Abnormal menstrual bleeding or abnormal periods
- Allergies to foods, dyes, or preservatives

Or if you are:

- pregnant or may be pregnant
- breastfeeding

Lastly, don't forget to tell your doctor about all the medicines you may be taking, including prescription drugs, vitamins, over-the-counter medications, and dietary and herbal supplements.

### In what pregnancy drug category is Clomid?

Clomid is in **Category X** which means studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

### If Clomid is so risky, how do women trying to get pregnant not take Clomid while they are pregnant?

To avoid inadvertent Clomid administration during early pregnancy, appropriate tests should be utilized during each treatment cycle to determine whether ovulation occurs. Women should be evaluated carefully to exclude pregnancy, ovarian enlargement, or ovarian cyst formation between each treatment cycle. The next course of Clomid therapy should be delayed until these conditions have been excluded.

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### What are Clomid birth defect risks?

If Clomid is taken during pregnancy, the risks of the following birth defects increase:

- Congenital heart lesions
- Down's syndrome
- Club foot
- Cleft lip and/or cleft palate
- Undescended testes in males
- Blindness
- Spina bifida
- Hernia
- Malformations
- Lifelong disability
- Death

### Have there been any calls to action by the FDA regarding Clomid?

The Potential Signals of Serious Risks/New Safety Information Identified from the Adverse Event Reporting System (AERS) between October and December 2008 notes the following:

#### CLOMIPHENE CITRATE (CLOMID)

##### *Visual Disorders*

FDA is evaluating this issue to determine if the labeling, which includes visual disorders in the Warnings and Adverse Reactions sections, is adequate.

The appearance of Clomid on this list does not mean that the FDA has concluded that the drug has the listed risk. It means that FDA has identified a *potential safety issue*, but does not mean that FDA has identified a causal relationship between the drug and the listed risk. If after further evaluation the FDA determines that the drug is associated with the risk, it may take a variety of actions including requiring changes to the labeling of the drug, requiring development of a Risk Evaluation and Mitigation Strategy (REMS), or gathering additional data to better characterize the risk.

### What are the visual problems associated with Clomid?

Blurring or other visual symptoms such as spots or flashes may sometimes occur during the use of Clomid. These symptoms increase per incidence or duration and usually disappear within a few days or weeks after Clomid is discontinued. These visual symptoms may make driving a car or operating machinery more hazardous than usual.





### Do you have more questions? Do you need resources?

For questions and resources about cleft lip and cleft palate, please contact: [The Cleft Lip and Palate Foundation of Smiles](#). Cleft lip or palate is one of the most common birth defects, currently affecting one in 600 children in the United States. The Foundation was formed by a young mother of twins both born with cleft lip and palate. The Foundation offers positive support to parents of children with craniofacial differences by offering news, information on cleft palate teams, [state by](#)

[state resources](#), [birth registry listings](#), and a [online community](#) where you can [register to meet other families](#) in your local area who are going through the same or similar concerns and where you can share and express useful information.

Do you want more information about Clomid, fertility drugs, and birth defects? Do you question whether taking Clomid to get pregnant caused your baby's birth defect? These are difficult questions to ask. Please contact [Rachel Mancuso](#) for assistance.

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### References

#### [Pharmacodynamics](#)

Reefhuis J, Honein MA, Schieve LA, Rasmussen SA; National Birth Defects

Prevention Study. Use of clomiphene citrate and birth defects, National Birth

Defects Prevention Study, 1997–2005. Hum Reprod. 2011 Feb;26 (2):451–7. Epub 2010; Nov 26. PubMed PMID: 21112952

Additional results: Clomiphene citrate use was reported by 1.4% of control mothers (94/6500). Among 36 case-groups assessed, increased adjusted odds ratios (aOR) were found [all: aOR, 95% confidence interval (CI)] for anencephaly (2.3, 1.1–4.7), Dandy-Walker malformation (4.4, 1.7–11.6), septal heart defects (1.6, 1.1–2.2), muscular ventricular septal defect (4.9, 1.4–16.8), coarctation of aorta (1.8, 1.1–3.0), esophageal atresia (2.3, 1.3–4.0), cloacal exstrophy (5.4, 1.6–19.3), craniosynostosis (1.9, 1.2–3.0) and omphalocele (2.2, 1.1–4.5).

#### [Drug information online](#)

Potential Signals of Serious Risks/New Safety Information Identified from the Adverse Event Reporting System (AERS) [FDA—Guidance, Compliance, Regulatory Information, Surveillance, Adverse Drug Effects](#)

#### [Pregnancy eMed-TV](#)

Side effects, precautions, warnings

### Other Research from The Cleft Lip & Palate Foundation of Smiles

Research and Recent Studies:

[Causes of Cleft Lip and Palate: Birth Defects](#)

[Causes of Cleft Lip and Palate: Health Insurance](#)

[Causes of Cleft Lip and Palate: Hydrocodone](#)

[Causes of Cleft Lip and Palate: Special Education](#)

[Causes of Cleft Lip and Palate: SSRIs](#)

[Causes of Cleft Lip and Palate: Topamax](#)