CAI | Contraceptive Access Initiative

The Food and Drug Administration's 10-Month Clock to Weigh Over-the-Counter Status for Oral Contraceptives

Two pharmaceutical companies are on the precipice of a historic step: seeking Food and Drug Administration (FDA) approval to make an oral contraceptive product available over-the-counter (OTC), after years of preparation and study behind the scenes.

Submitting a formal application would start a 10-month clock for the FDA to review the data on safety and effectiveness and decide whether to approve or deny the product for OTC status. The FDA has a strong track record of meeting this 10-month deadline, but a failure to do so in this case would be a troubling sign. Because the FDA treats most information about drug applications as confidential, outside stakeholders must rely on information released by the pharmaceutical company as a means to monitor the FDA's progress and verify that the agency follows the scientific evidence and does not bow to political pressure to delay approval or impose unjustified restrictions.

Oral contraceptives have 60 years of safety evidence; the over-the-counter review process is designed to ensure consumers can accurately follow the label instructions.

Potential Concerns

Two pharmaceutical companies are currently working to bring oral contraceptive products over-the-counter (OTC) in the United States: a progestin-only product (often referred to as a "mini-pill") and a combined, estrogen and progestin, oral contraceptive product. Both companies have been in talks with the FDA since 2016, according to the New York Times, and at least one of them may submit a formal application in 2022 for what would be a groundbreaking advance for contraceptive access.[1]

One big question surrounding such a historic move is whether the FDA or senior administration officials might delay or deny approval for political reasons, rather than making a decision based purely on the science. These concerns stem in part from the history of the emergency contraceptive Plan B, which was approved for unrestricted OTC status in 2013 only after more than a decade of delays, political interference, litigation and the imposition of age restrictions that were not justified by science and not recommended by career staff.[2,3,4]

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[1] https://www.nytimes.com/2021/12/14/business/birth-control-pill-over-counter.html?referringSource=articleShare
[2] https://www.verywellhealth.com/the-history-of-emergency-contraception-906714
[3] https://journalofethics.ama-assn.org/article/inappropriate-obstructions-access-fdas-handling-plan-b/2014-04
[4] https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-decision-regarding-plan-b-questions-and-answers

FDA Process

The process for moving a drug from prescription-only status to OTC status (an "Rx-to-OTC switch") includes many steps prior to submitting a formal application to the FDA. Typically, the pharmaceutical company discusses a development plan with the FDA and then conducts studies of consumers' ability to understand a proposed label ("label comprehension studies"), to identify whether the drug is appropriate for them ("self-selection studies"), and to safely and effectively use the drug in an OTC setting ("actual use trials").

Leading medical institutions, public health leaders and 59 members of Congress have urged the FDA to consider the pill OTC applications without delay or interference.

In this pre-application phase the FDA has wide latitude to make certain recommendations and requirements that significantly shape the approval process, the timeline for a product being moved over-the-counter and the medical standards that guide the consumer experience. Typically only after responding to the FDA's input and recommended criteria would the company file a formal application. This phase takes years to complete.

It is only after a formal application is submitted to the FDA that the timeline for an Rx-to-OTC switch becomes clear: The FDA has 10 months to make a decision to approve or deny the product for OTC status.[5] This 10-month timeframe comes from performance goals that the FDA has set for itself after negotiation with outside stakeholders, at the behest of Congress.[6,7]

This 10-month timeline includes numerous internal steps and deadlines for FDA staff.[8] Key steps include:

- Day 60: the deadline for the FDA to officially "file" the application (meaning, accept and review it) or reject the application as incomplete.
- Day 74: a "filing communication" letter is sent to the applicant, which describes any preliminary issues identified by FDA staff during their initial review and informs the applicant of the planned timeline.
- Month 5: FDA staff hold an internal, mid-cycle meeting. The FDA might (but is not required to) provide an update to the applicant afterward.
- Month 7 or 8: an FDA Advisory Committee would likely be held. Advisory Committee meetings are not required for all new drug applications, but they are standard for first-in-class nonprescription products,[9] which would be the case for an oral contraceptive product. Briefing materials would be released to the public at least two days prior to the Advisory Committee meeting.[10]
- End of month 10: the deadline for the FDA to provide a response to the applicant, either to approve or reject the application. If rejected, the FDA would provide a "complete response" letter, which describes the problems identified by the FDA and its recommendations for how the applicant could address them in a resubmitted application.

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[5] The timeline would be different for some drug applications, but those circumstances do not appear to apply in the case of oral contraceptives. For example, there is no reason to expect that they would be marked for a quicker "priority review," and they are not new molecular entities, which are subject to an extended review timeline.

[6] https://www.fda.gov/media/99140/download

[7] https://www.gao.gov/assets/gao-20-244.pdf

[8] https://www.fda.gov/media/78941/download

[9] https://www.fda.gov/media/72730/download

[10] https://www.fda.gov/media/75436/download

One potential way the 10-month timeline could be extended is if the pharmaceutical company submits a major amendment to its application — such as new analyses or studies — in the middle of the process. In that case, the FDA has the option of extending the timeline by three months.[11]

Transparency

Few, if any, of these steps — including the submission of an application in the first place — are necessarily transparent to the general public because the FDA generally treats information about drug applications as business confidential information. Specifically, FDA regulations legally prohibit the agency from making information about an application public until the application has been approved — unless it has already been "publicly disclosed or acknowledged" (as it has for both companies seeking FDA approval for an OTC pill). In that case, the FDA might disclose limited information to the public such as, "a summary of selected portions of the safety and effectiveness data that are appropriate for public consideration of a specific pending issue; for example, for consideration of an open session of an FDA advisory committee."[12]

Two pharmaceutical companies have been pursuing over-the-counter status for more than six years; one may submit a formal application soon.

However, the pharmaceutical company that submitted the application may choose to publicize its application and any number of other steps in the approval process. In fact, in the vast majority of cases, companies do announce that they have filed an application via a press release, filings with the Securities and Exchange Commission or both. One study found that this was true for 89% of new drug applications between 2010 and 2016, including 98% of new drug applications in 2016.[13]

Overall, most information about a future oral contraceptive OTC application is likely to come from the pharmaceutical company. An Advisory Committee meeting appears to be the most likely step in the process for the FDA to make public key information about the data submitted and the analysis by FDA reviewers.

FDA Track Record

The FDA's track record on the pre-application process is unclear because those deliberations and processes are typically hidden from public view. However, once a formal application has been submitted, the FDA's track record for meeting its 10-month timeline has been strong in recent years: The FDA approved 20 applications for Rx-to-OTC switches between January 2011 and March 2022.[14] Only one[15] of those applications took longer than 10 months, according to an analysis of approval documents on the FDA's website.[16]

[11] https://www.fda.gov/media/78941/download
[12] https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-314#314.430
[13] https://www.statnews.com/2019/06/04/hiding-plain-sight-nda-disclosure/
[14] https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/prescription-over-counter-otc-switch-list
[15] Voltaren Arthritis Pain, which took about 14 months; the circumstances around the delay are not in the public record.
[16] https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm

The agency has had a similar history with new drug applications more broadly, beyond Rx-to-OTC switches. According to the FDA's most recent annual statistics, for FY 2020, the agency acted within 10 months on 55 of 58 applications (95%) for the relevant category of applications.[17] In fact, the FDA met its deadlines at least 85% of the time for all types of applications.

The FDA has a very strong record in meeting the 10 month deadline for OTC switch applications. Of the 20 submitted over the past eleven years, 19 were approved by that deadline.

It is important to keep in mind that although the FDA has a strong recent history of meeting its deadlines to make a decision about drug applications, not all of those applications were approved. Between 63% and 67% of standard new drug applications (i.e., those not given priority review) were approved during their original cycle of review between FY 2014 and FY 2019 (the most recent year for which final data are available).[18] Applications that are not approved initially may be resubmitted by the pharmaceutical company for further FDA consideration, after taking steps to address any problems the FDA identified.

In summary, it would be unusual and therefore worrisome if the FDA failed to meet its 10-month deadline for making a decision on an Rx-to-OTC application for an oral contraceptive product. In fact, the FDA itself has intimated as much. According to the *New York Times*, the FDA "declined to answer specific questions" about the potential applications, but said it "aims to make a decision within 10 months once any company submits an application for approval of a move from prescription to over-the-counter status."[19]

Conclusion

When a pharmaceutical company submits a formal application to move an oral contraceptive product from prescription-only status to OTC status, it will be an exciting step in the history of contraceptive access in the United States. This step will trigger a 10-month deadline to approve or reject the application that the FDA only rarely misses.

The submission of an application will also mark a time period for outside stakeholders to scrutinize the FDA's actions and to demand as much transparency as possible from the pharmaceutical company and the FDA. Advocating for a public Advisory Committee and releasing comprehensive briefing materials will allow for greater scrutiny by the public of both the process and the evidence. Because of the agency's shameful history with emergency contraception, advocates for reproductive health and rights and others who care about the integrity of the FDA will want to trust but verify that the agency is following the scientific evidence in making its decisions and not bowing to political pressure for delays or restrictions.

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[17] https://www.fda.gov/media/156077/download
[18] https://www.fda.gov/media/156077/download
[19] https://www.nytimes.com/2021/12/14/business/birth-control-pill-over-counter.html?referringSource=articleShare