

First Script Prescription Benefit News for Workers' Compensation

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Ask The Pharmacist

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Beyond convenience, are there advantages in the use of fixed-dose combination drug products?

Fixed-dose combination drug products (FDCDPs) are made up of two different drug ingredients in a single formulation, containing a fixed amount of each. Among the more recognizable examples of these are Symbicort[®] (budesonide-formoterol) for management of asthma symptoms, Suboxone[®] (buprenorphine-naloxone) used in the treatment of opioid use disorder, Claritin D[®] (loratidine-pseudoephedrine) for treatment of symptoms of allergic or respiratory symptoms, and Tylenol PM[®] (acetaminophen – diphenhydramine) for symptom management in common cold, flu, or allergies. The list is very long, and these drugs are offered in both prescription and over-the-counter (OTC) versions.

Ideally, these combination products would offer a proven advantage in treatment effectiveness, safety, or adherence over the single ingredients administered separately.¹ Though it may seem safe to assume that marketers of FDCDPs could simply combine proven ingredients, relabel, and offer the product for sale, it is not often that simple. Even combinations of well-known drug ingredients with long-standing use must be submitted for approval with studies that demonstrate the contribution of each ingredient to the claimed therapeutic effect.² FDCDPs are often an opportunity for manufacturers to extend the market exclusivity of an OTC brand or a prescription brand whose patent is expiring.

Advantages of FDCDPs may include:²

- Improved effectiveness of the combination vs. either ingredient alone. Individual ingredients may treat the same symptom or condition but offer different mechanisms of action.
- Lower doses of individual ingredients in FDCDP than either agent used alone to achieve similar treatment effects, which may minimize side effects.
- Reduced pill burden and related improvements in patient adherence to medication regimens may result in improved treatment outcomes.

Disadvantages of FDCDPs may include:²

- Fixed amount/ratio of ingredients may be unsuitable or inadequate to treat a condition and may not allow dosage flexibility to individualize an effect.
- Caregiver and consumer lack of familiarity with the combination product.
- Inadvertent duplication of therapy may introduce potential for toxicity or overdose.
- Identifying the ingredient cause for an experienced adverse event is more difficult for combination products.
- Pricing for combination products may be significantly greater than either ingredient alone.

Some examples of FDCDPs in popular use include:

- An antibiotic, amoxicillin combined with clavulanic acid (a beta-lactamase inhibitor) that improves the performance of amoxicillin in the presence of some resistant bacterial strains.
- HIV combination therapy products that combine ingredients with demonstrated synergy for treatment of HIV.
- Levodopa-carbidopa combinations for the management of symptoms in Parkinson's Disease.

FDCDPs may offer effectiveness or convenience advantages that depend on the unique dimensions of a clinical scenario. The decision to use one or not hinges on a thorough understanding of their advantages and limitations. Pharmacists are thoroughly trained and well positioned to assist in identifying self-care symptoms and conditions that are best managed by single therapy or by an FDCDP.

1. Drug Development and Delivery – Accessed at: <https://drug-dev.com/fixed-dose-combinations-fixed-dose-combination-products-a-review-part-1-introduction/>
2. British Journal of Clinical Pharmacology – BrJ Clin Pharmacol. 2008 May;65(5) 785-796 – Accessed at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2432494/>

Drug of the Month

Advil® Dual Action with Acetaminophen

The Advil® product line has announced a new OTC medication offering to be introduced in 2020.¹ It is called Advil Dual Action with Acetaminophen and is a fixed-dose combination drug product, meaning each caplet contains two of the most widely consumed analgesics in the U.S., acetaminophen (250mg) and ibuprofen (125mg). This formula will be the first Food and Drug Administration (FDA) approved OTC product offered in the U.S. that combines these two analgesics for adults and children over 12 years of age.

In studies submitted for FDA approval of Advil Dual Action with Acetaminophen, the results supported a pain relief indication and also indicated superior analgesic effectiveness compared to either ingredient alone at the same dose.¹ The prescribing information for the product contains warnings that include those commonly observed for acetaminophen (liver damage) and ibuprofen (stomach bleeding).²

Ibuprofen and acetaminophen act to relieve pain by different pharmacologic mechanisms, which may help explain why the demonstrated effect of their combination in studies was greater than either ingredient alone. Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that acts by interfering with the release of pain-signaling prostaglandin substances at the pain source, while acetaminophen is thought to dampen the transmission of pain signals reaching the brain.

One advantage of this medication is that the combined activity of the ingredients may offer greater relief than either drug taken alone at similar doses. The recommended dose is two caplets every eight hours and may not reduce the total number of doses per day, compared with taking similar doses of each ingredient separately.² Other considerations include inadvertent use of many other prescribed or OTC medications containing ibuprofen or acetaminophen that could contribute to the potential for adverse effects or overdose toxicity. At the time of this publication, pricing information for Advil Dual Action with Acetaminophen was not available to allow a fuller assessment of cost effectiveness.

1. FDA approves GSK's Advil Dual Action with Acetaminophen for over-the-counter use in the United States (news release) @GSK.com – Accessed at: <https://www.gsk.com/en-gb/media/press-releases/fda-approves-gsk-s-advil-dual-action-with-acetaminophen-for-over-the-counter-use-in-the-united-states/>
2. Advil Dual Action with Acetaminophen Label – Accessed at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/211733Orig1s000lbl.pdf



Governmental Activity by State

Find out more about the governmental updates and potential changes currently being proposed in your state

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