

## 米国におけるコデイン含有医療用医薬品の 18 歳未満への使用制限について

平成 30 年 3 月 15 日  
医薬安全対策課

## 1 概要

平成 30 年 1 月 11 日、米国食品医薬品局（FDA : Food and Drug Administration）は、副作用の危険性（モルヒネ中毒<sup>（注1）</sup>）等から、コデイン又はヒドロコドン<sup>（注2）</sup>を含有する医療用鎮咳・風邪薬の 18 歳未満の患者への使用を制限する旨を発表した。なお、いくつかの州で販売されているコデインを含有する OTC についての規制措置は検討中としている。

（注1）コデインは、体内でモルヒネ（医療用麻薬）に代謝されることにより鎮咳等の薬効を示す。ヒドロコドンもオピオイドの一種でモルヒネ様の作用がある。

（注2）ヒドロコドンの日本国内での承認はない。

## 2 日本におけるコデイン類含有医薬品に関する小児等への投与制限の状況

コデイン類含有医薬品について、平成 29 年 4 月、小児の呼吸抑制発生リスク等の副作用を踏まえ、米国で 12 歳未満の小児への使用を制限する措置がとられたこと等を受け、平成 29 年 6 月に開催された平成 29 年度第 3 回安全対策調査会にて審議を行い、結論の概要は以下の通りである。

＜平成 29 年度第 3 回安全対策調査会での結論の概要＞

- （1）コデイン類含有医薬品の国内における使用は限定的であり、死亡例も報告されていないこと、国内における小児の呼吸抑制のリスクは欧米と比較して遺伝学的に低いと推定されること等から、国内で直ちに使用を制限する必要性は考えにくい。
- （2）一方、規制の国際的な整合性や、コデイン類含有医薬品による小児の呼吸抑制発生リスクを可能な限り低減する観点から、医療用医薬品・OTC とも、予防的な措置として以下の注意喚起等を行うことが適当。
  - ・ 速やかに添付文書を改訂し、12 歳未満の小児に使用しないよう注意喚起し、医療関係者にこの内容を周知する。
  - ・ 1 年 6 ヶ月程度の経過措置期間を設け、製造販売業者に、コデイン類を含まない代替製品や、12 歳未満の小児を適応外とする製品への切換えを行わせる。
  - ・ その後、12 歳未満の小児への使用を禁忌とする。

平成 29 年 7 月に「コデインリン酸塩水和物又はジヒドロコデインリン酸塩を含有する医薬品の小児に係る用法・用量の取扱い等について」（平成 29 年 7 月 4 日付け薬生薬審発 0704 第 3 号・薬生安発 0704 第 6 号厚生労働省医薬・生活衛生局医薬品審査管理課長・安全対策課長連名通知）を発出し、現在は上記予防的措置の経過措置期間中であり、最終的に 12 歳未満の小児への使用を禁忌とする方針である。医療用医薬品においては、平成 30 年 3 月現在で多くの製品が 12 歳未満の小児を適応外とする一変承認済みである。

### 3 コデイン類含有医薬品に関する各国の小児等への投与制限の状況

各国の状況は以下の通り。

	医療用医薬品	O T C 医薬品
E U	鎮痛・鎮咳目的：12 歳以上使用可	鎮痛・鎮咳目的：12 歳以上使用可
米国	扁桃腺除去術後の疼痛管理の目的： 18 歳以上使用可 鎮痛・鎮咳目的：12 歳以上使用可に限定 (平成 29 年 4 月) <u>今回</u> 鎮咳・風邪薬：18 歳以上使用可に限定 (平成 30 年 1 月)	鎮咳目的：2 歳以上使用可 (業界の自主的措置として 4 歳以上使用可として上市)
カナダ	鎮痛・鎮咳目的：12 歳以上使用可 (ただし扁桃腺除去術に係る疼痛管理の場合は 18 歳以上使用可)	鎮痛・鎮咳目的：12 歳以上使用可

### 4 日本における対応

- 米国の措置については、米国内のオピオイド濫用への対策の一環との指摘があること。
- 国内の 12-18 歳において、中毒関連症例に関する副作用報告がないこと。
- 小児の使用制限対象年齢の拡大について、米国以外では平成 30 年 3 月現在、実施されていないこと。
- 国内では平成 29 年 7 月に 12 歳未満の小児に使用しないよう注意喚起したばかりで、経過措置期間中である国内にて追加措置をとることにより、医療現場に混乱を招く懸念があること。

上記の状況に鑑み、コデイン類含有医薬品の投与制限の年齢の引き上げについては、当面、諸外国や国内での使用状況及び規制状況の推移を見守り、慎重に検討をおこなってはどうか。

## FDA requires labeling changes for prescription opioid cough and cold medicines to limit their use to adults 18 years and older

This provides updated information to the [FDA Drug Safety Communication: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women](#) issued on April 20, 2017.

### Safety Announcement

[1-11-2018] The U.S. Food and Drug Administration (FDA) is requiring safety labeling changes for prescription cough and cold medicines containing codeine or hydrocodone to limit the use of these products to adults 18 years and older because the risks of these medicines outweigh their benefits in children younger than 18. We are also requiring the addition of safety information about the risks of misuse, abuse, addiction, overdose, death, and slowed or difficult breathing to the *Boxed Warning*, our most prominent warning, of the drug labels for prescription cough and cold medicines containing codeine or hydrocodone.

We are taking this action after conducting an extensive review and convening a [panel of outside experts](#). Both of these determined the risks of slowed or difficult breathing, misuse, abuse, addiction, overdose, and death with these medicines outweigh their benefits in patients younger than 18.

**Health care professionals** should be aware that FDA is changing the age range for which prescription opioid cough and cold medicines are indicated. These products will no longer be indicated for use in children, and their use in this age group is not recommended. Health care professionals should reassure parents that cough due to a cold or upper respiratory infection is self-limited and generally does not need to be treated. For those children in whom cough treatment is necessary, alternative medicines are available. These include over-the-counter (OTC) products such as dextromethorphan, as well as prescription benzonatate products.

**Parents and caregivers** should be aware that prescription opioid cough and cold medicines that include codeine or hydrocodone should not be used in children. Codeine and hydrocodone are narcotic medicines called opioids and may carry serious risks when used in children. It is important for parents and caregivers to understand that a cough due to a common cold often does not need medicines for treatment. If a cough medicine is prescribed, ask your child's health care professional or a pharmacist if it contains an

opioid such as codeine or hydrocodone. Always read the labels on prescription bottles. If the medicine prescribed for your child contains an opioid, talk to your child’s health care professional about a different, non-opioid medicine, or if you have any questions or concerns.

Codeine and hydrocodone are available in combination with other medicines, such as antihistamines and decongestants, in prescription medicines to treat coughs and symptoms associated with allergies or the common cold. Other non-opioid prescription and OTC medicines are available to treat these symptoms.

Other *Boxed Warnings* and *Warnings and Precautions* will also be added to the label for prescription cough and cold medicines containing codeine or hydrocodone, to be consistent with the safety issues described in the labels of prescription opioid pain medicines. We previously communicated about these safety issues for [immediate-release opioid pain medicines](#) and [extended-release and long-acting opioid pain medicines](#).

Today’s action is for opioid cough and cold medicines requiring a prescription. Some codeine cough medicines are available OTC in a few states, and we also are considering regulatory action for these products.

We urge health care professionals and patients to report side effects involving opioid cough and cold medicines or other medicines to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

### List of Prescription Cough and Cold Medicines Containing Codeine

Active Ingredient(s)	Brand Name(s)
codeine, chlorpheniramine	Tuxarin ER, Tuzistra XR
codeine, phenylephrine, promethazine	Only generics available
codeine, promethazine	Only generics available
codeine, pseudoephedrine, tripolidine	Triacin C

### List of Prescription Cough and Cold Medicines Containing Hydrocodone

Active Ingredient(s)	Brand Name(s)
hydrocodone, guaifenesin	FlowTuss, Obredon
hydrocodone, pseudoephedrine, guaifenesin	Hycofenix, Rezira
hydrocodone, chlorpheniramine	Tussionex Pennkinetic, Vituz
hydrocodone, chlorpheniramine, pseudoephedrine	Zutripro
hydrocodone, homatropine	Only generics available

### Additional Information for Parents/Caregivers and Patients

- FDA is requiring labeling changes for prescription cough and cold medicines containing the opioid medicines codeine or hydrocodone to limit their use to adults 18 years and older because the risks of these medicines for cough outweigh

their benefits in children younger than 18. These risks include slowed or difficult breathing, misuse, abuse, addiction, overdose, and death.

- Always read the labels on prescription bottles to find out if a medicine contains codeine or hydrocodone, or ask your child's health care professional or a pharmacist.
- If your child is currently prescribed a cough and cold medicine containing codeine or hydrocodone, talk to your child's health care professional about other treatments.
- Common side effects of opioids include drowsiness, dizziness, nausea, vomiting, constipation, shortness of breath, and headache.
- Opioids also carry serious risks, including that these medicines depress the central nervous system, which can cause serious breathing problems or death. They can be used to get "high" or may result in someone becoming addicted to them.
- If you are an adult currently prescribed a cough and cold medicine containing codeine, hydrocodone or any other opioid, do not use these with other medicines that depress the central nervous system (CNS) without discussing it with your health care professional. Alcohol also depresses the CNS and can increase the risk for these serious and life-threatening side effects.
- Do not take more of these medicines than the dose prescribed or listed on the label, as doing so can cause serious problems.
- Always use an accurate measuring device to measure and administer liquid medicines. If you are not sure how to measure liquid medicines, ask a pharmacist for help.
- Breastfeeding is not recommended during treatment with opioid cough and cold medicines, because the medicine passes through breast milk and can harm the baby.
- Always tell your health care professionals about all the medicines you or your child are taking, including over-the-counter (OTC) medicines.
- Always [lock up medicines](#) and [dispose](#) of them properly when no longer needed to keep them from being taken accidentally by children or teenagers or falling into the wrong hands.
- Read the patient [Medication Guide](#) or patient information leaflet that comes with filled prescription(s).
- If you have any questions or concerns about a medicine you or your child has been prescribed, talk with your health care professional or your pharmacist.
- Report side effects from opioid cough and cold medicines or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

## **Related Information**

[Codeine Information](#)

[Opioid Medications](#)

[Expert Roundtable Meeting: Use of Cough Suppressants in Children](#)

[Disposal of Unused Medicines: What You Should Know](#)

[The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective](#)

[Think It Through: Managing the Benefits and Risks of Medicines](#)

[Advisory Committees: Critical to the FDA's Product Review Process](#)