**LEVODROPROPIZINE** ( MEWELL )

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| **Pharmacological Properties:** |
| The cough is a defense reflex responding to chemical, mechanical and/or bacterial stimulation of the tracheobronquial system. The risk to control the cough reflex lies in the suppression of the productive cough, which helps to clear the airways. The cough that should be controlled is the non-productive cough since this type of cough does not help clear bronchial passages. There are several centrally acting antitussives suppressing this reflex; however, they can cause significant effects on the central nervous system. Peripheral antitussive drugs act on chemical and mechanical receptors mainly located in the larynx and trachea lacking effects on the central nervous system, which make them more tolerable. Levodropropizine is the L-enantiomer of dropropizine, a racemic non-opiate antitussive agent.    **PHARMACOKINETICS** Levodropropizine is rapidly absorbed and distributed after oral administration. The bioavailability of levodropropizine is 75% and the half life time is 1-2 hours. Levodropropizine is 11-14% human plasma proteins bound. Levodropropizine is mainly excreted through the urinary route, both as an unaltered product and in the way of metabolites: conjugated levodropropizine and free and conjugated p-hydroxy levodropropizine. After 48 hours, the excretion of the product and the indicated metabolites is close to 35% of the administered dose. There are no significant alterations in the pharmacokinetic profile of children and elderly patients, and of patients affected by a mild to moderate renal failure.   **MECHANISM OF ACTION** Levodropropizine is a peripherally acting agent inhibiting the afferent pathways that mediate the generation of the cough reflex. Compared with the racemic drug, levodropropizine maintains the antitussive activity but considerably lower central nervous system depressant actions.  Its mechanism of action is mainly peripheral at the tracheobronquial level, although it is also associated to some antialergic and anti bronchospastic activity.  Levodropropizine does not affect the respiratory center, hence it can be used in patients having respiratory depression together with non-productive cough.  Levodropropizine is activated in the bronchopulmonary system as the inhibitor of bronchospasm induced by histamine, serotononin and bradiquinine. |
| **Indications:** |
| **Symptomatic treatment of non-productive cough**. |
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| **Dosage and Administration:**  Administration Route: Oral Usual Dose: Adults and children over 12 years of age: 10 mL of syrup 3 times daily at least every 6 hours.  Children over 2 years of age: pediatric dose is 1 mg / kg every 8 hours; administer dose at least every 6 hours. |
| **Contraindications:** |
| Levodropropizine is contraindicated in patients with hypersensitivity to the active ingredient or any of the components of the formulation.  It is also contraindicated in patients suffering from bronchorrhea or having an altered mucociliary function (Kartagener syndrome, primary ciliary dyskinesia). Levodropropizine is also contraindicated during pregnancy and while breastfeeding. |
| **Precautions and Warnings:** |
| Since this medication may cause, although rarely, somnolence, patients should be advised not to drive or operate machinery. Do not administer to children under 2 years of age. Caution should be exercised in patients suffering from a severe renal failure (creatinine clearance lower than 35 mL/min) and in elderly patients.    **PREGNANCY AND BREASTFEEDING** Teratogenic studies involving reproduction and fertility, and perinatal and postnatal studies do not show specific toxic effects. However, since in toxicological animal studies a mild decrease in body weight and growth has been observed, and since levodropropizine passes through the placental barrier of rats, pregnant women or women who are trying to get pregnant should avoid using this drug because the safety of levodropropizine in pregnancy has not been evaluated.  Studies in rats have shown that this medication is excreted in breast milk after 8 hours of being administered. Therefore, the use of this medication while breastfeeding is not recommended. |
| **Adverse Reactions:** |
| Nausea, pyrosis, dyspepsia, diarrhea, vomiting, fatigue and/or asthenia, somnolence, headache, vertigo and palpitations may occasionally occur but disappear when the treatment is discontinued. Skin allergy has been rarely observed. |
| **Interactions:** |
| No interactions have been reported, however, caution should be taken when using levodropropizine concomitantly with sedatives. |
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| **De Blasio *et al.* *Cough* 2011 7:7   doi:10.1186/1745-9974-7-7** |

**The American College of Chest Physicians (ACCP) issued their evidence based "Guidelines on Cough" in 2006, which state that anti-tussive drugs related with therapy of acute or chronic bronchitis showing the highest level of benefit were levodropropizine and moguisteine, that act through a peripheral mechanism, while the central antitussive drugs such as codeine and dextromethorphan showed a lower level of benefit**

**American College of Chest Physicians (ACCP):**

**Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. Chest 2006, 129:1S-23S.**

**Poster Presentations** | **October 2011**

# Cough Incidence, Impact on Sleep, and Antitussive Treatment in the Pediatric Population FREE TO VIEW

Alessandro Zanasi, MD; Luigi Lanata; Gianluca De Danieli; Filippo Bernardi, PhD; Salvatore Cazzato; Francesco De Blasio

***Chest****.*2011; 140(4\_MeetingAbstracts):383A. doi:10.1378/chest.1118177

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## Abstract

**PURPOSE:** Cough is one of the most frequent symptoms in children, affecting up to 25% of children of school and preschool age, and is one of the most common reasons for which children are visited by primary care pediatricians.

**METHODS:** Overall, 433 children requiring pediatrician consultation for acute cough due to upper respiratory tract infection were enrolled in this observational study. Cough epidemiology, sleep quality and antitussive treatment were evaluated. Cough severity and frequency were assessed at baseline and after 6 days through a questionnaire administered to parents. Multivariate analysis was performed on treatment outcomes.

**RESULTS:**  The mean age of children was 6.1 years. Cough incidence was 12.2%. Cough disturbed sleep in 87.5% of children and 71% of parents. The number of children treated with peripheral antitussive (levodropropizine, n=101) was higher than with central cough suppressants (codeine and cloperastine, n=60). Both classes of drugs were effective in reducing cough intensity and frequency. However, the percentage of cough resolution was significantly higher with levodropropizine than with central antitussives (47% vs. 28% respectively, p=0.0012). The percentage of no change/worsening was only 3% for levodropropizine vs. 18% for central drugs. In any type of cough (dry, productive or mixed), multivariate analysis showed a much higher probability of cough resolution/improvement for levodropropizine (90-95%) vs. central antitussives (60-85%) vs. other therapy/no treatment (50-80%), independently from the use of antibiotics and concomitant diseases.

**CONCLUSIONS:** Cough significantly disturbed children and parents sleep. The peripheral antitussive levodropropizine was the most used drug by pediatricians for children cough treatment. A significant advantage was observed for levodropropizine in terms of higher cough resolution and lower unsuccessful treatment, independently from cough intensity. In multivariate analysis, levodropropizine showed the highest probability of cough resolution/improvement.

**CLINICAL IMPLICATIONS:** Empiric treatment with antitussive agents is often needed in children. **Peripheral antitussive levodropropizine seems to be the best therapeutic option, while centrally acting cough suppressants, although largely used, have no consistent evidence of efficacy and there are increasing reports of association with serious adverse events in children.**

**DISCLOSURE:** Alessandro Zanasi: Grant monies (from industry related sources): This project was founded by Dompé S.P.A.

Luigi Lanata: Employee: Dompé S.P.A.

Gianluca De Danieli: Employee: Dompé S.P.A.

Filippo Bernardi: Grant monies (from industry related sources): This project was founded by Dompé S.P.A.

# Efficacy of levodropropizine in pediatric cough.

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[**Pulmonary Pharmacology &amp Therapeutics**](http://www.researchgate.net/journal/1522-9629_Pulmonary_Pharmacology_amp_Therapeutics) (impact factor: 2.8). 07/2012; 25(5):337-42. DOI:10.1016/j.pupt.2012.05.010

Source: [PubMed](http://www.ncbi.nlm.nih.gov/pubmed/22771902)

**ABSTRACT** Cough in children is among the most common problems managed by pediatricians, and occurs more frequently in preschool than in older children. Most acute episodes of cough are due to viral upper respiratory tract infections. The morbidity associated with acute cough in a child extends also to parents, teachers, and other family members and caregivers. Unfortunately, therapeutic options for acute cough in children are severely limited due to the absence of drugs shown to be effective antitussives with an acceptable safety profile. Agents used in the management of adult cough, such as narcotics (codeine, hydrocodone), the non-narcotic opioid dextromethorphan, first-generation, potentially sedating antihistamines, and decongestants such as pseudoephedrine, have all been deemed inadequate for treatment of acute pediatric cough on a risk/benefit basis. A growing body of evidence suggests that the peripherally acting antitussive, levodropropizine, may be an attractive alternative for the treatment of bothersome acute cough in children.