PRESCRIBING INFORMATION

INCLUDING PATIENT MEDICATION INFORMATION

ⓃNOVAHISTEX® DH

Hydrocodone bitartrate - Phenylephrine HCl

Syrup, hydrocodone bitartrate 5 mg - phenylephrine HCl 20 mg

Antitussive - Decongestant

sanofi-aventis Canada Inc.
2905 Place Louis-R.-Renaud
Laval, Quebec H7V 0A3

Date of Revision:
November 14, 2019

Submission Control No.: 226615

s-a Version 4.0 dated November 14, 2019

TABLE OF CONTENTS

ℕNOVAHISTEX® DH

Hydrocodone bitartrate - Phenylephrine HCl

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	Syrup, hydrocodone bitartrate 5 mg and phenylephrine HCl 20 mg per 5 mL	Amaranth color, artificial raspberry flavour, artificial taste modifier, citric acid, liquid glucose, glycerine, menthol, propylene glycol, purified water, sodium benzoate, sodium chloride, sodium citrate, sodium cyclamate and xylitol. Alcohol free. ***For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section.***

INDICATIONS AND CLINICAL USE

Adults
NOVAHISTEX DH is indicated for the treatment of adults with cough associated with inflamed mucosa, which does not respond to products of lesser potency.

Geriatrics (> 65 years of age)
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, concomitant disease or other drug therapy.

Pediatrics (<18 years of age)
NOVAHISTEX DH is not indicated for use in patients younger than 18 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of hydrocodone to hydromorphone and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of hydrocodone in these patients (see also **CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, Respiratory, Special Populations, Pediatrics**; and **DOSAGE AND ADMINISTRATION**).

CONTRAINDICATIONS

- Children younger than 6 years of age.
- Patients who are hypersensitive to the active substance hydrocodone bitartrate and phenylephrine HCl or other opioid analgesics or to any ingredient in the formulation. For a complete listing, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the Prescribing Information.
- In patients with known or suspected mechanical gastrointestinal obstruction (e.g., bowel obstruction or strictures) or any diseases/conditions that affect bowel transit (e.g., ileus of any type).
- Patients with suspected surgical abdomen (e.g., acute appendicitis or pancreatitis).
- Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus.
- Patients with acute respiratory depression, elevated carbon dioxide levels in the blood and cor pulmonale.
- Patients with acute alcoholism, delirium tremens, and convulsive disorders.
- Patients with severe CNS depression, increased cerebrospinal or intracranial pressure, and head injury.
- Patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy).

WARNINGS AND PRECAUTIONS

SERIOUS WARNINGS AND PRECAUTIONS

Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the risks of overdose and death with immediate release opioid formulations, NOVAHISTEX DH (hydrocodone bitartrate and phenylephrine HCl) should only be used in patients for whom alternative non-opioid treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide appropriate cough management (see DOSAGE AND ADMINISTRATION).

Addiction, Abuse, and Misuse
NOVAHISTEX DH poses risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Each patient's risk should be assessed prior to prescribing NOVAHISTEX DH, and all patients should be monitored regularly for the development of these behaviors or conditions (see WARNINGS AND PRECAUTIONS, Abuse and Misuse). NOVAHISTEX DH should be stored securely to avoid theft or misuse.

Life-threatening Respiratory Depression: OVERDOSE
Serious, life-threatening, or fatal respiratory depression may occur with use of

NOVAHISTEX DH. Infants exposed *in-utero* or through breast milk are at risk of life-threatening respiratory depression upon delivery or when nursed. Patients should be monitored for respiratory depression, especially during initiation of NOVAHISTEX DH or following a dose increase. Further, instruct patients of the hazards related to taking opioids including fatal overdose.

Accidental Exposure
Accidental exposure to NOVAHISTEX DH, especially by children, can result in a fatal overdose of hydrocodone bitartrate (see DOSAGE AND ADMINISTRATION, Disposal, for instructions on proper disposal).

Neonatal Opioid Withdrawal Syndrome
Prolonged maternal use of NOVAHISTEX DH during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening (see WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome (NOWS)).

Interaction with Alcohol
The co-ingestion of alcohol with NOVAHISTEX DH should be avoided as it may result in dangerous additive effects, causing serious injury or death (see WARNINGS AND PRECAUTIONS and DRUG INTERACTIONS).

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death (see WARNINGS AND PRECAUTIONS, Neurologic).

- **Reserve concomitant prescribing of NOVAHISTEX DH and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

General

Before prescribing medication to suppress or modify cough, it is important to ascertain that the underlying cause of the cough is identified, that modification of the cough does not increase the risk of clinical or physiological complications, and that appropriate therapy for the primary disease is provided.

Accidental ingestion, especially by children can result in a fatal overdose of hydrocodone bitartrate (see DOSAGE AND ADMINISTRATION, disposal, for instructions on proper disposal).

Patients should be instructed not to give NOVAHISTEX DH (hydrocodone bitartrate) to anyone other than the patient for whom it was prescribed, as such inappropriate use may

have severe medical consequences, including death. NOVAHISTEX DH should be stored securely to avoid theft or misuse.

Patients should be cautioned not to consume alcohol while taking NOVAHISTEX DH as it may increase the chance of experiencing serious adverse events, including death.

Administer with caution to patients hypersensitive to sympathomimetic preparations, patients with hyperthyroidism, diabetes mellitus and glaucoma.

Abuse and Misuse

Like all opioids, **NOVAHISTEX DH** is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, **NOVAHISTEX DH** should be prescribed and handled with caution.

Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse and abuse.

Use in Drug and Alcohol Addiction

NOVAHISTEX DH is an opioid with no approved use in the management of addictive disorders. Its proper usage in individuals with drug or alcohol dependence, either active or in remission, is for the management of cough requiring opioids. Patients with a history of addiction to drugs or alcohol may be at higher risk of becoming addicted to NOVAHISTEX DH; extreme caution and awareness is warranted to mitigate the risk.

Cardiovascular

Hydrocodone bitartrate administration may result in hypotension and dizziness.

Administer with caution to patients with severe hypertension, cardiac or peripheral vascular disease.

Dependence/Tolerance

As with other opioids, tolerance and physical dependence may develop upon repeated administration of NOVAHISTEX DH and there is a potential for development of psychological dependence.

Physical dependence and tolerance reflect the neuroadaptation of the opioid receptors to chronic exposure to an opioid, and are separate and distinct from abuse and addiction. Tolerance, as well as physical dependence, may develop upon repeated administration of opioids, and are not by themselves evidence of an addictive disorder or abuse.

Continuous dosage over extended periods of time may cause a hydrocodone bitartrate dependent state.

Patients on prolonged therapy could experience withdrawal symptoms following abrupt discontinuation of therapy or upon administration of an opioid antagonist. Some of the symptoms

that may be associated with abrupt withdrawal of an opioid include body aches, diarrhea, gooseflesh, loss of appetite, nausea, nervousness or restlessness, anxiety, runny nose, sneezing, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in sweating, palpitations, unexplained fever, weakness and yawning (see **ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage).**

Endocrine

Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

Gastrointestinal Effects

Hydrocodone bitartrate and other morphine-like opioids have been shown to decrease bowel motility. Patients with chronic constipation should be given the drug only after weighing the potential therapeutic benefit against the hazards involved. Hydrocodone bitartrate may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Neonatal Opioid Withdrawal Syndrome (NOWS)

NOVAHISTEX DH is not recommended to be used in pregnant women unless, in the judgement of the physician, the potential benefits outweigh the risks. If NOVAHISTEX DH was used during pregnancy, special attention to NOWS is warranted.

Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening.

Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhea and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the newborn.

Neurologic

Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol): Concomitant use of opioids, including NOVAHISTEX DH, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Because of these risks, avoid use of opioid cough medications in

patients taking benzodiazepines, other CNS depressants, or alcohol (see DRUG INTERACTIONS).

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with concomitant use of opioid cough medications and benzodiazepines, other CNS depressants, or alcohol.

Advise both patients and caregivers about the risks of sedation and respiratory depression if NOVAHISTEX DH is used with benzodiazepines, alcohol, or other CNS depressants.

NOVAHISTEX DH should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects, including death (see **CONTRAINDICATIONS** and **DRUG INTERACTIONS, Drug-Lifestyle Interactions**).

Use in Patients with Convulsive or Seizure Disorders: The hydrocodone bitartrate in NOVAHISTEX DH may aggravate convulsions in patients with convulsive disorders, and may induce or aggravate seizures in some clinical settings. Therefore, NOVAHISTEX DH should not be used in these patients (see **CONTRAINDICATIONS**).

Serotonin Syndrome: NOVAHISTEX DH could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs (e.g. anti-depressants, migraine medications). Treatment with the serotonergic drug should be discontinued if such events (characterized by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. NOVAHISTEX DH should not be used in combination with MAO inhibitors or serotonin-precursors (such as L-tryptophan, oxitriptan) and should be used with caution in combination with other serotonergic drugs (triptans, certain tricyclic antidepressants, lithium, tramadol, St. John's Wort) due to the risk of serotonergic syndrome.

Head Injury: The respiratory depressant effects of hydrocodone bitartrate, and the capacity to elevate cerebrospinal fluid pressure, may be greatly increased in the presence of an already elevated intracranial pressure produced by trauma. Also, hydrocodone bitartrate may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of patients with head injury. In such patients, hydrocodone bitartrate must be used with extreme caution and only if it is judged essential (see **CONTRAINDICATIONS).**

Psychomotor Impairment

NOVAHISTEX DH may impair the mental and/or physical abilities needed for certain potentially hazardous activities such as driving a car or operating machinery. Patients should be cautioned accordingly. Patients should also be cautioned about the combined effects of hydrocodone bitartrate and/or phenylephrine HCl with other CNS depressants effects during antihistaminic therapy, including other opioids, phenothiazine, sedative/hypnotics and alcohol.

Respiratory

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression from opioid use, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status. NOVAHISTEX DH should be used with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia (see **CONTRAINDICATIONS**).

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of NOVAHISTEX DH, the risk is greatest during the initiation of therapy or following a dose increase. Patients should be closely monitored for respiratory depression when initiating therapy with NOVAHISTEX DH and following dose increases.

Hydrocodone bitartrate, including NOVAHISTEX DH is not recommended for use in any patient in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, lung infections, multiple trauma or extensive surgical procedures.

Life-threatening respiratory depression is more likely to occur in the elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients.

Hydrocodone, including NOVAHISTEX DH, is not indicated for patients under 18 years of age. Hydrocodone is contraindicated in patients below the age of 6 years. In young children, the respiratory centre is especially susceptible to the depressant action of narcotic cough suppressants. The use of hydrocodone bitartrate in children less than 6 years of age has been associated with fatal respiratory depression. A 5 year old child treated for cough died after a few hours of exposure to hydrocodone bitartrate; the child was a CYP2D6 poor metabolizer and was concomitantly exposed to clarithromycin, a CYP3A4 inhibitor and valproic acid, a broad-spectrum inhibitor of the uridine diphosphate glucoronosyltransferases (UGTs), resulting in blood hydrocodone levels associated with fatality. Such a scenario of hydrocodone overdose can be equally plausible in CYP2D6 intermediate, extensive, and ultrarapid metabolizers, especially in the presence of other drug interactions and physical vulnerabilities for children up to 18 years of age and adults. Exercise caution when administering NOVAHISTEX DH because of the potential for respiratory depression. If respiratory depression occurs, discontinue and use naloxone hydrochloride when indicated to antagonize the effect and other supportive measures as necessary.

Use in Patients with Chronic Pulmonary Disease: Monitor patients with significant chronic obstructive pulmonary disease or cor pulmonale, and patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression for respiratory depression, particularly when initiating therapy and titrating with NOVAHISTEX DH, as in these patients, even usual therapeutic doses of NOVAHISTEX DH may decrease respiratory drive to the point of apnea. The use of NOVAHISTEX DH is contraindicated in patients with

acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus (see **CONTRAINDICATIONS**).

Sexual Function/Reproduction

Long-term use of opioids may be associated with decreased sex hormone levels and symptoms such as low libido, erectile dysfunction, or infertility (see **ADVERSE REACTIONS, Post-Marketing Experience**).

Special Populations

Special Risk Groups: Hydrocodone bitartrate should be administered with caution to patients with a history of alcohol and drug abuse and in a reduced dosage to debilitated patients, and in patients with severely impaired pulmonary function, Addison's disease, hypothyroidism, myxedema, toxic psychosis, prostatic hypertrophy or urethral stricture.

Pregnant Women: Studies in humans have not been conducted. NOVAHISTEX DH crosses the placental barrier and is not recommended to be administered to pregnant women unless in the judgement of the physician, potential benefits outweigh the risks.

Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal Opioid Withdrawal Syndrome (NOWS), unlike opioid withdrawal syndrome in adults, can be life-threatening (see **WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome**).

Pregnant women using opioids should not discontinue their medication abruptly as this can cause pregnancy complication such as miscarriage or still-birth. Tapering should be slow and under medical supervision to avoid serious adverse events to the fetus.

Labour, Delivery and Nursing Women: Since opioids can cross the placental barrier and are excreted in breast milk, NOVAHISTEX DH is not recommended to be used in nursing women and during labour and delivery unless, in the judgement of the physician, the potential benefits outweigh the risks. Life-threatening respiratory depression can occur in the infant if opioids are administered to the mother. Naloxone, a drug that counters the effects of opioids, should be readily available if NOVAHISTEX DH is used in this population.

Pediatrics (<18 years of age): NOVAHISTEX DH is not indicated for use in patients younger than 18 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of hydrocodone to hydromorphone and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of hydrocodone in these patients (see **INDICATIONS AND CLINICAL USE** and **DOSAGE AND ADMINISTRATION**).

NOVAHISTEX DH is contraindicated in children younger than 6 years of age. In young children, the respiratory centre is especially susceptible to the depressant action of narcotic cough suppressants

Geriatrics (> 65 years of age): In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range and titrate slowly, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see **DOSAGE AND ADMINISTRATION**).

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The most frequently observed adverse reactions of NOVAHISTEX DH are:
Occasional drowsiness, dry mouth, dizziness, blurred vision, mild mental stimulation and gastric irritation may occur rarely.

Post-Marketing Experience

Other adverse reactions reported with the use of cough and cold medications include: convulsions, hallucinations, allergic reaction, breathing difficulties, rapid heart rate, reflex bradycardia and urinary retention.

Androgen deficiency: Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date. Patients presenting with symptoms of androgen deficiency should undergo laboratory evaluation.

DRUG INTERACTIONS

Overview

Interaction with Benzodiazepines and Other Central Nervous System (CNS) Depressants (including alcohol): Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants (e.g. other opioids, sedatives/hypnotics, antidepressants, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, phenothiazines, neuroleptics, antihistamines, antiemetics, and alcohol) and beta-blockers, increases the risk of respiratory depression, profound sedation, coma, and death and should be avoided (see **WARNINGS AND PRECAUTIONS, Neurologic, Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol) and Psychomotor Impairment)**. NOVAHISTEX DH should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

Drug-Drug Interactions

Serotonergic Agents: Coadministration of hydrocodone bitartrate with a serotonergic agent, such as a Selective Serotonin Re-uptake Inhibitor or a Serotonin Norepinephrine Re-uptake Inhibitor, may increase the risk of serotonin syndrome, a potentially life-threatening condition (see **WARNINGS AND PRECAUTIONS, Neurologic**).

Inhibitors of CYP3A4 and CYP2D6: The concomitant use of NOVAHISTEX DH and CYP3A4 inhibitors, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g. ketoconazole), or protease inhibitors (e.g., ritonavir), can increase the plasma concentration of hydrocodone, resulting in increased or prolonged opioid effects. These effects could be more pronounced with concomitant use of NOVAHISTEX DH and CYP2D6 and CYP3A4 inhibitors, particularly when an inhibitor is added after a stable dose of NOVAHISTEX DH is achieved. Avoid the use of NOVAHISTEX DH while taking a CYP3A4 or CYP2D6 inhibitor. If concomitant use is necessary, monitor patients for respiratory depression and sedation at frequent intervals.

Drug-Lifestyle Interactions

Patients should be cautioned not to operate vehicles or hazardous machinery until their response to the drug has been determined.

The concomitant use of alcohol should be avoided (see **WARNINGS AND PRECAUTIONS, General**).

DOSAGE AND ADMINISTRATION

Pediatrics (<18 years of age):
NOVAHISTEX DH is not indicated for use in patients younger than 18 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of hydrocodone to hydromorphone and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of hydrocodone in these patients. NOVAHISTEX DH is contraindicated in children younger than 6 years of age.

Increasing Risk with Higher Doses
All doses of opioids carry an inherent risk of fatal or non-fatal adverse events. This risk is increased with higher doses. The recommended maximum daily dose of NOVAHISTEX DH is 30 mL (30 morphine milligram equivalent). Each patient should be assessed for their risk prior to prescribing NOVAHISTEX DH, as the likelihood of experiencing serious adverse events can depend upon the type of opioid and duration of treatment, as well as the patient's own level of tolerance. In addition, the coughing should be assessed routinely to confirm the most appropriate dose and the need for further use of NOVAHISTEX DH.

Recommended Dose and Dosage Adjustment

Adults:
5 mL every 4 hours. Do not use for longer than 7 days.

Geriatrics:
Respiratory depression has occurred in the elderly following administration of large initial doses of opioids to patients who were not opioid-tolerant or when opioids were co-administered with other agents that can depress respiration. NOVAHISTEX DH should be initiated at a low dose and slowly titrated to effect (see **WARNINGS AND PRECAUTIONS**).

Adjustment or Reduction of Dosage: Physical dependence with or without psychological dependence tends to occur with chronic administration of opioids, including NOVAHISTEX DH. Withdrawal (abstinence) symptoms may occur following abrupt discontinuation of therapy. These symptoms may include body aches, diarrhea, gooseflesh, loss of appetite, nausea, nervousness or restlessness, runny nose, sneezing, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in sweating, palpitations, unexplained fever, weakness and yawning.

Missed Dose
If the patient forgets to take one or more doses, they should take their next dose at the next scheduled time and in the normal amount.

Disposal
NOVAHISTEX DH should be kept in a safe place, out of the sight and reach of children before, during and after use. NOVAHISTEX DH should not be used in front of children, since they may copy these actions.

NOVAHISTEX DH should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired NOVAHISTEX DH should be properly disposed of as soon as it is no longer needed to prevent accidental exposure to others, including children or pets. If temporary storage is required before disposal, a sealed child-proof container, such as a biohazard waste container or lockable medication box could be obtained from a pharmacy.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Symptoms: Symptoms are similar to those caused by overdosage of hydrocodone. Narcosis is usually present, sometimes associated with convulsions. Tachycardia, pupillary constriction, nausea and vomiting or respiratory depression can occur.

Treatment: If respiration is severely depressed, administer the narcotic antagonist, naloxone.

Adults: 400 μg by i.v., i.m. or s.c. routes and repeated at 2 to 3 minute intervals if necessary.

Children: 10 μg/kg by i.v., i.m. or s.c. routes. Dosage may be repeated as for the adult administration. Failure to obtain significant improvement after 2 to 3 doses suggests that causes other than narcotic overdosage may be responsible for the patient's condition.

If naloxone is unsuccessful, institute intubation and respiratory support or conduct gastric lavage in the unconscious patient.

STORAGE AND STABILITY
Store between 15 – 30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Composition:
Each 5 mL of red, raspberry-flavored liquid contains: hydrocodone bitartrate 5 mg and phenylephrine HCl 20 mg.

Non-medicinal ingredients: amaranth color, artificial raspberry flavour, artificial taste modifier, citric acid, liquid glucose, glycerine, menthol, propylene glycol, purified water, sodium benzoate, sodium chloride, sodium citrate, sodium cyclamate and xylitol. Alcohol free.

Packaging:
Bottles of 100 mL and 500 mL.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:
Hydrocodone bitartrate and phenylephrine HCl

Chemical name:
Hydrocodone bitartrate: 4,5-Epoxy-3-methoxy-17-methyl-5alpha-morphinan-6-one (2R,3R)-2,3-dihydroxybutanedioate

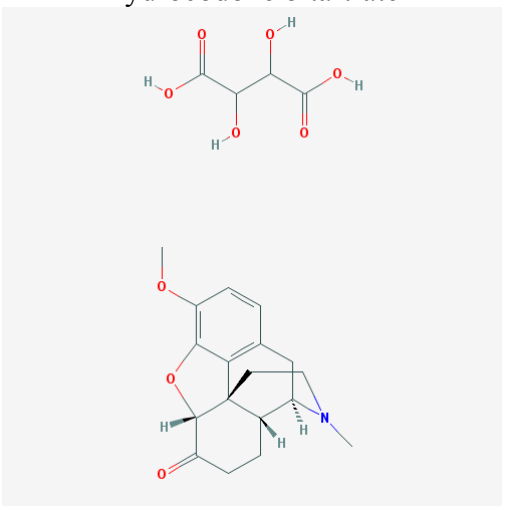
Phenylephrine HCl: 3-[(1R)-1-hydroxy-2-(methylamino)ethyl]phenol;hydrochloride

Molecular formula and molecular mass:

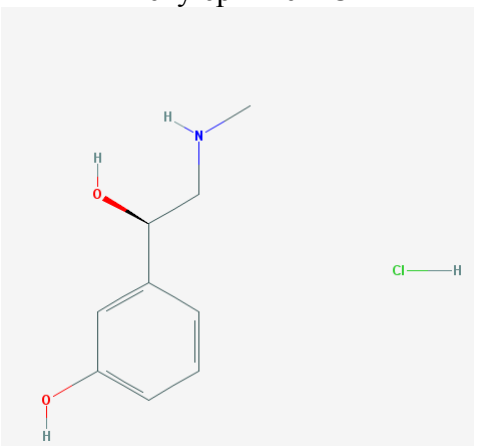
	Molecular formula	Molecular mass
Hydrocodone bitartrate	$C_{22}H_{27}NO_9$	449.45
Phenylephrine HCl	$C_9H_{14}ClNO_2$	203.67

Structural formula:

Hydrocodone bitartrate



Phenylephrine HCl



Physicochemical Properties:

Hydrocodone bitartrate: Odorless white crystalline powder. pH (2% aqueous solution) about 3.6.Melting Point: 294.8° F. Soluble in water (62 mg/mL water).

Phenylephrine HCl: Odorless white microcrystalline powder. Bitter taste. pH (1% aqueous solution) about 5. Melting Point: 284 to 293° F. Solubility greater than or equal to 100 mg/mL at 70° F.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

ℕNOVAHISTEX® DH

Hydrocodone bitartrate and phenylephrine HCl, syrup

Read this carefully before you start taking **NOVAHISTEX DH** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **NOVAHISTEX DH**.

Serious Warnings and Precautions

- **Even if you take NOVAHISTEX DH as prescribed you are at a risk for opioid addiction, abuse and misuse. This can lead to overdose and death.**
- **You may get life-threatening breathing problems while taking NOVAHISTEX DH. This is less likely to happen if you take it as prescribed by your doctor. Babies are at risk of life-threatening breathing problems if their mothers take opioids while pregnant or nursing.**
- **You should never give anyone your NOVAHISTEX DH. They could die from taking it. If a person has not been prescribed NOVAHISTEX DH, taking even one dose can cause a fatal overdose. This is especially true for children.**
- **If you took NOVAHISTEX DH while you were pregnant, whether for short or long periods of time or in small or large doses, your baby can suffer life-threatening withdrawal symptoms after birth. This can occur in the days after birth and for up to 4 weeks after delivery. If your baby has any of the following symptoms:**
  - **has changes in their breathing (such as weak, difficult or fast breathing)**
  - **is unusually difficult to comfort**
  - **has tremors (shakiness)**
  - **has increased stools, sneezing, yawning, vomiting, or fever**

  Seek immediate medical help for your baby.
- **Taking NOVAHISTEX DH with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.**

What is NOVAHISTEX DH used for?

NOVAHISTEX DH is a prescription medicine for adults, used to treat cough associated with colds that is not responding to other medications.

NOVAHISTEX DH is not for use in patients younger than 18 years of age. In patients this age, the risks of life-threatening breathing problems outweigh the benefits of treating the cough with hydrocodone.

How does NOVAHISTEX DH work?

NOVAHISTEX DH contains two ingredients, hydrocodone bitartrate and phenylephrine HCl.

Hydrocodone bitartrate helps suppress cough by acting on the cough center in the brain. Phenylephrine HCl works by constricting blood vessels in the nasal passages, helping to relieve nasal congestion.

What are the ingredients in NOVAHISTEX DH?

Medicinal ingredients: Hydrocodone bitartrate and phenylephrine HCl
Non-medicinal ingredients: Amaranth color, artificial raspberry flavour, artificial taste modifier, citric acid, liquid glucose, glycerine, menthol, propylene glycol, purified water, sodium benzoate, sodium chloride, sodium citrate, sodium cyclamate and xylitol. Alcohol free.

NOVAHISTEX DH comes in the following dosage forms:

Syrup, hydrocodone bitartrate 5 mg and phenylephrine HCl 20 mg per 5 mL

Do not use NOVAHISTEX DH if:

- your doctor did not prescribe it for you
- you are allergic to hydrocodone bitartrate and phenylephrine HCl or to any of the other ingredients in NOVAHISTEX DH (see **What are the ingredients in NOVAHISTEX DH?**), or other opioid analgesics
- you have severe asthma, trouble breathing, or other breathing problems
- you have any heart problems
- you have bowel blockage or narrowing of the stomach or intestines
- you have severe pain in your abdomen
- you have a head injury
- you have a brain tumor
- you are at risk for having seizures
- you suffer from alcoholism
- you are going to have, or recently had, a planned surgery
- you are taking or have taken within the past 2 weeks a Monoamine Oxidase inhibitor (MAOi) (such as phenelzine sulphate, tranylcypromine sulphate, moclobemide or selegiline)

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take NOVAHISTEX DH. Talk about any health conditions or problems you may have, including if you:

- have a history of illicit or prescription drug or alcohol abuse
- have severe kidney, liver or lung disease
- have diabetes
- have glaucoma
- have heart problems or peripheral vascular disease (problems with your blood vessels)
- have low blood pressure
- have high blood pressure
- have past or current depression
- suffer from chronic or severe constipation
- have problems with your thyroid, adrenal or prostate gland
- have, or had in the past hallucinations or other severe mental problems
- suffer from migraines
- are pregnant or planning to become pregnant

Other warnings you should know about:

Some people metabolize hydrocodone at a much faster rate than the general population. This which may lead to accidental overdose especially in patients younger than 18 years of age. Stop taking NOVAHISTEX DH and seek immediate medical help if you start feeling confused, have shallow breathing, or extreme sleepiness. If you know that you metabolize hydrocodone at a much faster rate, tell your doctor BEFORE starting this medication.

Stop taking NOVAHISTEX DH and consult with your healthcare professional if:

- you get a high fever, rash or persistent headache while taking NOVAHISTEX DH along with the cough.
- your symptoms or cough worsen or continue for more than 7 days.

These could be signs of a serious condition.

Use in Children
Young children are at greater risk of the sedating effects of narcotic cough drugs. The use of hydrocodone in young children has led to slow, shallow or weak breathing that has been fatal. **NOVAHISTEX DH** is not for use in patients younger than 18 years of age.

Opioid dependence and addiction:
As with all opioids, taking NOVAHISTEX DH may cause you to become dependent on it. Do not take more than the dose prescribed to you by your doctor. There are important differences between physical dependence and addiction. It is important that you talk to your doctor if you have questions or concerns about abuse, addiction or physical dependence. As with all opioids, taking hydrocodone may cause you to become dependent on it. Do not take more than the dose prescribed to you by your doctor.

Pregnancy, nursing, labour and delivery:
Opioids can be transferred to your baby through breast milk, or while still in the womb. NOVAHISTEX DH can then cause life-threatening breathing problems in your unborn baby or nursing infant. Your doctor will determine if the benefits of using NOVAHISTEX DH outweigh the risks to your unborn baby or nursing infant.

If you are pregnant and are taking NOVAHISTEX DH, it is important that you don't stop taking your medication all of a sudden. If you do, it can cause a miscarriage or a still-birth. Your doctor will monitor and guide you on how to slowly stop taking NOVAHISTEX DH. This may help avoid serious harm to your unborn baby.

Driving and using machines: Before you do tasks which may require special attention, you should wait until you know how you react to NOVAHISTEX DH. NOVAHISTEX DH can cause:

- drowsiness
- dizziness or
- lightheadedness

This can usually occur after you take your first dose and when your dose is increased.

Serotonin Syndrome: NOVAHISTEX DH can cause Serotonin Syndrome, a rare but potentially life-threatening condition. It can cause serious changes in how your brain, muscles and digestive system work. You may develop Serotonin Syndrome if you take NOVAHISTEX DH with certain antidepressants or migraine medications.

Serotonin Syndrome symptoms include:

- fever, sweating, shivering, diarrhea, nausea, vomiting;
- muscle shakes, jerks, twitches or stiffness, overactive reflexes, loss of coordination;
- fast heartbeat, changes in blood pressure;
- confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.

Disorder of the adrenal gland: You may develop a disorder of the adrenal gland called adrenal insufficiency. This means that your adrenal gland is not making enough of certain hormones. You may experience symptoms such as:

- nausea, vomiting
- feeling tired, weak or dizzy
- decreased appetite

You may be more likely to have problems with your adrenal gland if you have been taking opioids for longer than one month. Your doctor may do tests, give you another medication, and slowly take you off NOVAHISTEX DH.

Sexual Function/Reproduction: Long term use of opioids may lead to a decrease in sex hormone levels. It may also lead to low libido (desire to have sex), erectile dysfunction or being infertile.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with NOVAHISTEX DH:

- alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking NOVAHISTEX DH. It can lead to:
    - drowsiness
    - unusually slow or weak breathing
    - serious side effects or
    - a fatal overdose
- other sedative drugs which may enhance the drowsiness caused by NOVAHISTEX DH
- opioid analgesics (drugs used to treat pain)
- general anesthetics (drugs used during surgery)
- benzodiazepines (drugs used to help you sleep or that help reduce anxiety)
- antidepressants (for depression and mood disorders). **Do not** take NOVAHISTEX DH with MAO inhibitors (MAOi) or if you have taken MAOi's in the last 14 days.
- drugs used to treat serious mental or emotional disorders (such as schizophrenia)
- anti-retroviral drugs (use to treat viral infections)
- anti-fungal drugs (used to treat fungal infections)
- antibiotic drugs (used to treat bacterial infections
- antihistamines (drugs used to treat allergies)
- anti-emetics (drugs used to prevent vomiting)
- drugs used to treat muscle spasms and back pain
- some heart medication (such as beta blockers)
- drugs used to treat migraines (e.g. triptans)
- St. John's Wort

How to take NOVAHISTEX DH:

- Your doctor will prescribe the lowest dose that works to control your symptoms.
- It is recommended that you only take NOVAHISTEX DH for up to 7 days. If you need to take NOVAHISTEX DH for longer, your doctor will determine the best dose for you to lower the risk of side effects and overdose. Higher doses can lead to more side effects and a greater chance of overdose.
- NOVAHISTEX DH may be taken with or without food.

Usual Dose:

Adults:
5 mL every 4 hours. Do not use for longer than 7 days.

Be sure to use NOVAHISTEX DH only for the condition for which it was prescribed.

If you develop any side effect as a result of taking NOVAHISTEX DH, tell your doctor immediately.

Stopping your Medication

If you have been taking NOVAHISTEX DH for more than a few days you may experience some of the following uncomfortable symptoms when you stop taking it:

- body aches
- diarrhea
- goosebumps
- loss of appetite
- nausea
- feeling nervous or restless
- runny nose
- sneezing
- tremors or shivering
- stomach cramps
- rapid heart rate (tachycardia)
- having trouble sleeping
- an unusual increase in sweating
- heart palpitations
- an unexplained fever
- weakness
- yawning

Refilling your Prescription for NOVAHISTEX DH:

A new written prescription is required from your doctor each time you need more NOVAHISTEX DH. Therefore, it is important that you contact your doctor before your current supply runs out.

Only obtain prescriptions for this medicine from the doctor in charge of your treatment. Do not seek prescriptions from other doctors unless you switch to another doctor.

Overdose:

If you think you have taken too much NOVAHISTEX DH, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Signs of overdose may include:

- unusually slow or weak breathing
- dizziness
- confusion
- extreme drowsiness

- convulsion
- tachycardia (heart palpitations)
- constriction of the pupils
- nausea
- vomiting

Missed Dose:
If you missed a dose of this medication, take it as soon as you remember. But if it is almost time for your next dose, skip the missed dose and continue with your next scheduled dose. Go back to the regular dosing schedule. Do not take two doses at the same time.

What are possible side effects from using NOVAHISTEX DH?
These are not all the possible side effects you may feel when taking NOVAHISTEX DH. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:
- drowsiness
- insomnia
- dizziness
- fainting
- nausea, vomiting, or a poor appetite
- dry mouth
- headache
- problems with vision
- weakness, uncoordinated muscle movement
- itching
- light-headedness
- sweating
- constipation
- mild mental stimulation
- convulsions
- urinary retention
- low sex drive, impotence (erectile dysfunction), infertility

Talk with your doctor or pharmacist about ways to prevent constipation when you start using NOVAHISTEX DH.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
RARE **Overdose:** hallucinations, confusion, inability to walk normally, slow or weak breathing, extreme sleepiness, sedation, or dizziness, floppy muscles/low muscle tone cold and clammy skin, convulsion			✓
Respiratory Depression: slow, shallow or weak breathing			✓
Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
Bowel Blockage (impaction): abdominal pain, severe constipation, nausea			✓
Withdrawal: nausea, vomiting, diarrhea, anxiety, shivering, cold and clammy skin, body aches, loss of appetite, sweating		✓	
Fast, Slow or Irregular Heartbeat: heart palpitations		✓	
Low Blood Pressure: dizziness, fainting, light-headedness	✓		
Serotonin Syndrome: agitation or restlessness, loss of muscle control or muscle twitching, tremor, diarrhea			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- **Keep unused or expired NOVAHISTEX DH in a secure place to prevent theft, misuse or accidental exposure to children and pets.**
- **Keep NOVAHISTEX DH under lock, out of sight and reach of children and pets.**
- **Never take medicine in front of small children as they will want to copy you. Accidental ingestion by a child is dangerous and may result in death. If a child accidentally takes NOVAHISTEX DH, get emergency help right away.**
- Store at room temperature (15 – 30°C).

Disposal:

NOVAHISTEX DH should never be thrown into household trash, where children and pets may find it. It should be returned to a pharmacy for proper disposal.

If you want more information about NOVAHISTEX DH:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this consumer medication information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.sanofi.ca, or by calling 1-800-265-7927.

This leaflet was prepared by sanofi-aventis Canada Inc.

Last Revised: November 14, 2019