What Are Opioids?

Opioids are substances that act on opioid receptors to produce morphine-like effects. Medically they are primarily used for pain relief, including anesthesia. Other medical uses include suppression of diarrhea, replacement therapy for opioid use disorder, reversing opioid overdose, and suppressing cough.

They are class of drugs naturally found in the opium poppy plant and that work in the brain to produce a variety of effects, including the relief of pain with many of these drugs.

Opioids can be prescription medications often referred to as painkillers, or they can be so-called street drugs, such as heroin.

Many prescription opioids are used to block pain signals between the brain and the body and are typically prescribed to treat moderate to severe pain. In addition to controlling pain, opioids can make some people feel relaxed, happy or “high,” and can be addictive. Additional side effects can include slowed breathing, constipation, nausea, confusion and drowsiness.

OPIOIDS RECEPTOR

INTRODUCTION:

Receptors are proteins which are, by far the most important drug targets in medicine.
The Opioids Receptors belongs to family of **G-protein coupled receptors**. Morphine and other opioids exert their action by interacting with specific receptors present on neurons in the CNS and peripheral tissues.
The interaction of drug with receptor was analogous a "**Lock and Key**".
Agonist: An agent which activates receptors to produce a effect to that of the physiological signal molecules.
Antagonist: An agent which prevents the action of an agent on receptor but does not have any effect of its own.

TYPES OF OPIOIDS RECEPTOR:

The opioids receptors are mainly classified as three types

- Mu(μ) receptors
- Delta (δ) receptors
- Kappa (κ) receptors

1. Mu (μ) Receptors

- The Mu receptors are characterized by its high affinity for **morphine**.
- The endogenous ligand for Mu receptors peptides called **Endomorphine** and have recently found in mammalian brain.
- Endomorphine are endogenous opioids peptide with high degree of selectivity for Mu receptors.
- The 2 subtypes of Mu receptor are..
  Mu 1 receptor
  Mu 2 receptor

2. Delta (δ) Receptors

- In Delta receptors the Endomorphinehave less selectivity. Generally **Etorphine**, **Cyclozacine** and **levorphinol** are the agonist involved in Delta receptors.
- This receptors have less serious side effects as compare to Mu receptors.
- The 2 subtypes of Delta receptor are:
  Delta 1 receptor
  Delta 2 receptor

3. Kappa (κ) Receptors:

- The Kappa receptors define by its high affinity for **Ketocylcazocine** and **Dynorphin**.
- The 2 subtypes of Kappa receptor are:
  Kappa 1 receptor
  Kappa 2 receptor

OPIOID AGONIST:

MORPHINE

DEFINITION: Morphine is the major analgesic drug contained in crude opium and is the prototype strong agonist. Codeine is present in crude opium in lower concentrations and is inherently less potent, making codeine the prototype of the weak opioid agonists. Morphine and several other opioids have high affinity for μ receptors, whereas other agents have varying affinities for δ and κ receptors.

MECHANISM OF ACTION: Opioids exert their major effects by interacting with opioid receptors in the CNS and in other anatomic structures, such as the GI tract and the urinary bladder. Morphine acts at receptors in laminae I and II of the dorsal horn of the spinal cord, and it decreases the release of substance P, which modulates pain perception in the spinal cord.

ACTIONS:

a. **Analgesia:** Morphine causes analgesia (relief of pain without the loss of consciousness. Patients treated with morphine are still aware of the presence of pain, but the sensation is not unpleasant.

b. **Euphoria:** Morphine produces a powerful sense of contentment and wellbeing. Euphoria may be caused by disinhibition of the dopamine-containing neurons of the ventral tegmentum.

c. **Respiration:** Morphine causes respiratory depression by reduction of the sensitivity of respiratory center neurons to carbon dioxide. This can occur with ordinary doses of morphine in patients who are opioid-naïve and can be accentuated as the dose is increased until, ultimately, respiration ceases.

d. **GI tract:** Morphine relieves diarrhea and dysentery by decreasing the motility and increasing the tone of the intestinal circular smooth muscle. Morphine also increases the tone of the anal sphincter.Morphine can also increase biliary tract pressure due to contraction of the gallbladder and constriction of the biliary sphincter.

e. **Cardiovascular:** Morphine has no major effects on the blood pressure or heart rate except at large doses, at which hypotension and bradycardia may occur.

f. **Labor:** Morphine may prolong the second stage of labor by transiently decreasing the strength, duration, and frequency of uterine contractions.

PHARMACOKINETICS

a. Administration: Because significant first-pass metabolism of morphine occurs in the liver, intramuscular, subcutaneous, and IV injections produce the most reliable responses. Absorption of morphine from the GI tract is slow and erratic.

b. Distribution: Morphine rapidly enters all body tissues, including the fetuses of pregnant women, and should not be used for analgesia during labor. Infants born of addicted mothers show physical dependence on opiates and exhibit withdrawal symptoms if opioids are not administered.

c. Metabolism ;Once morphine reaches the bloodstream, it is carried to the liver where a large proportion of it is broken down, a process termed first-pass metabolism .In the case of subcutaneous injection, blood levels of morphine peak after about 20 minutes and with oral ingestion, levels peak after about 30 minutes.

d.Excretion: Around 90% of morphine taken is excreted from the body within 24 hours, mostly in the form of urine. Morphine has an elimination half-life of around 120 minutes. The drug can be stored in fat, so remains detectable for a long time after use and even after a person has died.

ADVERSE EFFECTS:

Severe respiratory depression can occur and result in death from acute opioid poisoning. A serious effect of the drug is stoppage of respiratory exchange in patients with emphysema. If used in such individuals, respiration must be carefully monitored. Other effects include vomiting, dysphoria, and histamine-enhanced hypotensive effects. The elevation of intracranial pressure, particularly in head injury, can be serious. Morphine enhances cerebral and spinal ischemia. In benign prostatic hyperplasia, morphine may cause acute urinary retention. Patients with adrenal insufficiency or myxedema may experience extended and increased effects from the opioids. Morphine should be used cautiously in patients with bronchial asthma, liver failure, or impaired renal function.

TOLERENCE:

Repeated use produces tolerance to the respiratory depressant, analgesic, euphoric, and sedative effects of morphine. However, tolerance usually does not develop to the pupil-constricting and constipating effects of the drug. Physical and psychological dependence readily occur with morphine and with some of the other agonists Withdrawal produces a series of autonomic, motor, and psychological responses that incapacitate the individual and cause serious (almost unbearable) symptoms. However, it is very rare that the effects are so profound as to cause death.

CODIENE:

DEFINITION: Codeine is an opioid pain reliever which is used to treat mild to moderately severe pain and to help reduce coughing. Codeine is available as a single ingredient tablet and also available in multi ingredients products combined with other pain relieving medicines or cold and flu medicines.

MECHANISM OF ACTION

The analgesic actions of codeine derive from its conversion to morphine by the CYP450 2D6 enzyme system, whereas the drug's antitussive effects are due to codeine itself. Binds to opioid receptors in the CNS, causing inhibition of ascending pain pathways, altering the perception of and response to pain; causes cough suppression by direct central action in the medulla; produces generalized CNS depression

PHARMACOKINETICS:

Absorption: Codeine, when administered as codeine sulfate, is absorbed from the gastrointestinal tract with maximum plasma concentration occurring 60 minutes post administration.

Distribution: Codeine has been reported to have an apparent volume of distribution of approximately 3-6 L/kg, indicating extensive distribution of the drug into tissues. Codeine has low plasma protein binding with about 7-25% of codeine bound to plasma proteins.

Metabolism: Hepatic via UGT2B7 and UGT2B4 to codeine-6-glucuronide, via CYP2D6 to morphine (active), and via CYP3A4 to norcodeine. Morphine is further metabolized via glucuronidation to morphine-3-glucuronide and morphine-6-glucuronide (active).

Excretion: Approximately 90% of the total dose of codeine is excreted through the kidneys, of which approximately 10% is unchanged codeine. Plasma half-lives of codeine and its metabolites have been reported to be approximately 3 hours.

ACTIONS:

General effects Codeine is a weak narcotic pain reliever and cough suppressant that is similar to morphine and hydrocodone. A small amount of ingested codeine is converted to morphine in the body. Codeine increases tolerance to pain, reducing existing discomfort.

Antitussive activity This drug has shown antitussive activity in clinical trials and has been effective in cough secondary to tuberculosis and insomnia due to coughing. Codeine suppresses the cough reflex through a direct effect on the cough center in the medulla.

Effects on intestinal motility Codeine may reduce intestinal motility through both a local and possibly central mechanism of action. This may possibly lead to constipation. The chronic use of opioids, including codeine sulfate, may lead to obstructive bowel disease, particularly in patients with underlying disorders of intestinal motility.

Effects on the central nervous system Codeine phosphate is an opioid analgesic with uses similar to those of morphine, but is much less potent as an analgesic. Its primary site of action is at the *mu* opioid receptors distributed throughout the central nervous system.

Effects on blood pressure: This drug poses an increased risk of compromised ability to maintain blood pressure due to peripheral vasodilation and other mechanisms

ADVERSE EFFECTS:

The most frequently observed adverse reactions include drowsiness light headedness, dizziness, sedation, shortness of breath, nausea, and constipation. Respiratory depression resulting in death has been reported in children who received codeine postoperatively following tonsillectomy and/or adenoidectomy. Heartbeat irregularities, blood pressure changes. Frequency not reported cases, bradycardia, tachycardia, edema**,** Drowsiness, dizziness, Headache, lightheadedness, feeling faint, paradoxical CNS stimulation (especially in children), disorientation, weakness and frequency not

reported. Seizures, Constipation, Dry mouth, loss of appetite, nausea, vomiting, paralytic ileus, toxic megacolon, anorexia, stomach cramps and at lower extent, gastrointestinal distress, anorexia, diarrhea, pancreatitis.

TOLERANCE: Codeine tolerance can develop quickly and increased dosages of any opioid drugs can lead to physical and/or psychological dependence. Increased tolerance to codeine may prompt the person to use other drugs or alcohol to intensify or enhance the medication's effects and this can cause serious physical and mental health impairments, overdose, or death. Tolerance to codeine medications poses additional health risks. When the medications are combined with acetaminophen, tolerance may lead the person to use much more than is safe and cause acetaminophen toxicity which can lead to liver failure and death.

OXYCODONE AND OXYMORPHONE:

It is a semisynthetic derivative of morphine. It is orally active and is sometimes formulated with aspirin or acetaminophen.

BRANDS:

Oxycodone:
Oxaydo , Roxicodone (immediate-release tablet)
Oxycontin (extended-release tablet)
Xtampza ER (ER capsule)
Oxymorphone:
Opana
Opana ER

USES:

- It is used to treat moderate to severe pain for example after an operation or a serious injury, or pain from cancer.
- It's also used for other types of long-standing pain when weaker painkillers, such as paracetamol, ibuprofen and aspirin, have not worked. It has many properties in common with morphine. Oxycodone is metabolized to products with lower analgesic activity.

EXCRETION:

- Excretion is via the kidney.
- Immediate-release formulations have average half-life of 3.2 hours.
- Controlled/extended-release formulations have a longer half-life of about 4.5 hours to 5.6 hours.

ADVERSE EFFECTS:

- Nausea, vomiting, constipation, light headedness, dizziness, or drowsiness may occur.

- Abuse of the sustained-release preparation (ingestion of crushed tablets) has been implicated in many deaths.
- It is important that the higher-dosage forms of the latter preparation be used only by patients who are tolerant to opioids

HYDROCODONE AND HYDROMORPHONE:

BRAND NAMES:

Hydrocodone:

- Hysingla ER
- Zohydro ER
- Hycodan

Hydromorphone:

- Dilaudid
- Exalgo

USES:

- Hydrocodone is only used to treat people who are expected to need medication to relieve severe pain around-the-clock for a long time.
- Hydromorphone extended-release capsules and extended-release tablets are used to relieve pain in opioid-tolerant patients

EXCRETION:

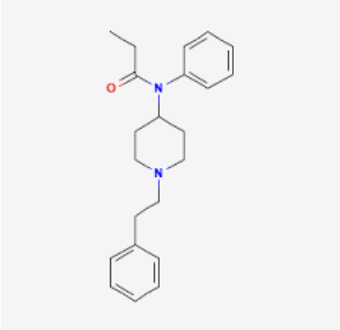
Hydrocodone:
It is metabolized in the liver by the P450 microsomal oxidizing enzyme system
Hydromorphone:
Metabolism occurs in the liver through glucuronidation where most of it converts to hydromorphone-3-glucuronide. Excretion is mainly through urine in the glucuronidated form.

ADVERSE EFFECTS:

- shallow or light breathing.
- constipation, which can be severe, especially with extended-release forms.
- Drowsiness, dizziness or lowered blood pressure, when standing up.
- Nausea, vomiting
- headache, mood changes.

FENTANYL:

- The most frequently employed opioids are fentanyl and its congeners, sufentanil or remifentanil, because they induce



analgesia more rapidly than morphine dose.Fentanyl is a powerful opioid used as a pain medication and, together with other medications for anesthesia.Sufentanil, alfentanil, and remifentanil arethree drugs related to fentanyl. Sufentanil is even more potent than fentanyl, whereas the other two are less potent but much shorter-acting.

BRANDS:

- Duragesic®, DTrans®; Fencino®; Fentalis®; Matrifen®; Mezolar®; Opiodur®

MECHANISM OF ACTION:

- Fentanyl metabolism occurs via cytochrome P450 (CYP34A) enzymes into inactive metabolites; hence drugs that enhance or inhibit cytochrome P450 will affect its metabolism.

USES:

- Epidural fentanyl is used for analgesia postoperatively and during labour. An oral transmucosal preparation and a transdermal patch are also available. The transmucosal preparation is used in the treatment of cancer patients with breakthrough pain who are tolerant to opioids. Fentanyl is often used during cardiac surgery because of its negligible effects on myocardial contractility. Muscular rigidity, primarily of the abdomen and chest wallis often observed with fentanyl use in anaesthesia.

ADVERSE EFFECT:

- Adverse effects of fentanyl are life-threatening hypoventilation, the fentanyl patch is contraindicated in the management of acute and postoperative pain or pain that can be ameliorated with other analgesics. It causes pupillary constriction.

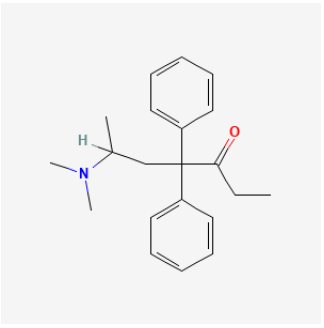
DOSES:

- The drug is highly lipophilic and has a rapid onset and short duration of action (15 to 30 minutes). It is usually injected IV, epidurally, or intrathecally.
- Surgery Premedication. 50-100 mcg/dose IM or slow IV 30-60 min prior to surgery. Adjunct to regional anesthesia: 25-100 mcg/dose slow IV 40-60 min.

METHADONE:

Methadone is a synthetic, orally effective opioid that is approximately equal in potency to morphine but induces less euphoria and has a somewhat longer duration of action.

BRANDS: Dolophine and Methadose



MECHANISM OF ACTION:

It is primarily a μ-receptor agonist and may mimic endogenous opioids, enkephalins, and endorphins and affect the release of other neurotransmittersacetylcholine, norepinephrine, substance P, and dopamine.Methadone also acts as an agonist of κ- and σ-opioid receptors, as an antagonist of the N-methyl-D-aspartate (NMDA) receptor,and as an inhibitor of serotonin and norepinephrine uptake.Specifically, by inhibiting the NMDA receptor, methadone dampens a major excitatory pain pathway within the central nervous system. Methadone effects on NMDA inhibition may explain its improved analgesic efficacy and reduced opioid tolerance.

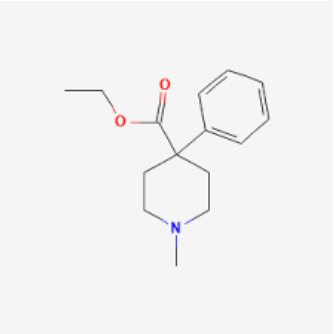
USES:

Methadone is used as an analgesic as well as in the controlled withdrawal of dependent abusers from heroin and morphine. Orally administered, methadone is substituted for the injected opioid. The patient is then slowly weaned from methadone. Methadone causes a withdrawal syndrome that is milder but more protracted (days to weeks) than that of other opioids.

ADERSE EFFECT:

- Methadone can produce physical dependence like that of morphine example:Heavy sweating, Constipation, Sexual problems, Weight gain.

MEPERIDINE:



Meperidine is a synthetic opioid structurally unrelated to morphine. It is used for acute pain.

BRANDS: Demerol, pethidine.

MECHANISM OF ACTION:

Meperidine binds to opioid receptors, particularly Âμ receptors. However, it also binds well to Îº receptors. Meperidine mimics the actions of endogenous neuropeptides via opioid receptors, thereby producing the characteristic morphine-like effects on the mu-opioid receptor, including analgesia, euphoria, sedation, respiratory depression, miosis, bradycardia and physical dependence.

USES:

Meperidine provides analgesia for any type of severe pain. Unlike morphine, meperidine is not clinically useful in the treatment of diarrhea or cough. Meperidine produces less of an increase in urinary retention than does morphine. It has significantly less effects on uterine smooth muscle than morphine and is the opioid commonly employed in obstetrics.

ADVERSE EFFECT:

Large or repetitive doses of meperidine can cause anxiety, tremors, muscle twitches, and rarely, convulsions due to the accumulation of a toxic metabolite, normeperidine. It dilates the pupil and causes hyperactive reflexes. Severe hypotension can occur when the drug is administered postoperatively. Due to its antimuscarinic action, patients may experience dry mouth and blurred vision. When used with major neuroleptics, depression is greatly enhanced. Administration to patients taking monoamine oxidase inhibitors can provoke severe reactions, such as convulsions and hyperthermia. Meperidine can cause dependence, and can substitute for morphine or heroin in opiate-dependent persons. Partial cross-tolerance with the other opioids occurs.

DOSES:

Meperidine is most often administered parenterally. The drug has a duration of action of 2 to 4 hours.

Pain: 50-150 mg. Intravenous (IV) injection: inject the dose of 10 mg/ml slowly

SUFENTANIL

Sufentanil, sold under the brand names Dsuvia and Sufenta, is a synthetic opioid analgesic drug approximately 5 to 10 times as potent as its parent drug, fentanyl, and 500 times as potent as morphine. Structurally, sufentanil differs from fentanyl through the addition of a methoxymethyl group on the piperidine ring (which increases potency but is believed to reduce duration of action and the replacement of the phenyl ring by thiophene. Sufentanil first was synthesized at Janssen Pharmaceutica.

MECHANISM OF ACTION:

Sufentanil is an opioid agonist and is relatively selective for the mu-opioid receptor, although it can bind to other opioid receptors at higher doses. The principle therapeutic action of sufentanil is analgesia and sedation, thought to be mediated through opioid-specific receptors throughout the CNS. Like all full opioid agonists, there is no ceiling effect to analgesia.

ADVERSE EFFECT:

- Nausea
- Headache
- Vomiting
- Dizziness
- Hypotension

DOSAGE:

Dosage Forms & Strengths injectable solution: Schedule II 0.05mg/mL.

ANESTHESIA:

Induction/intubation: 1-2 mcg/kg IV, THEN 10-50 mcg IV PRN.
General Anesthesia: 8-30 mcg/kg IV, THEN 25-30 mcg IV PRN.
Should be administered with 100% O2, with ventilatory support.
Dose should be calculated based on ideal body weight.

OTHER INDICATIONS AND USES:

Low dose: Analgesia in intubation, ventilation (adjunct).
High dose: Primary anesthesia induction & maintain Epidural analgesia (with bupivacaine).

ALFENTANIL

Alfentanil is a synthetic opioid analgesic. Alfentanil interacts predominately with the opioid mu-receptor. These mu-binding sites are discretely distributed in the human brain, spinal cord, and other tissues. In clinical settings, alfentanil exerts its principal pharmacologic effects on the central nervous system.

MECHANISM OF ACTION:

Alfentanil is of the opioid class of medications and thus acts by stimulation of the opioid receptors, of which there are three main subtypes: mu (m), kappa (k), and delta (d). The receptor primarily involved in pain transmission is the m-opioid receptor. The opioid receptors are predominately present in the central nervous system, brain, spinal column, and peripheral nervous system but are also present in vascular, cardiac, lung, gut, and even peripheral blood mononuclear cells. The natural ligands for the opioid receptors are called the “endogenous opioid peptides” and include enkephalins, endorphins, and Endomorphine.

DOSES:

In clinical trials, patient requirements have generally been met with doses of 0.5 to 10 mg Alfenatnil per hour. Additional bolus doses of 0.5 – 1.0 mg Alfenatnil may be given to provide analgesia during short painful procedures. The maximum recommended duration of treatment with alfentanil infusions is 4 days.

ADVERSE EFFECT:

Respiratory events reported during MAC included hypoxia, apnea, and bradypnea. Other adverse events reported by patients receiving Alfenatnil for MAC, in order of decreasing frequency, were nausea, hypotension, vomiting, pruritus, confusion, somnolence and agitation.

REMIFENTANIL

Remifentanil is a specific mu-type-opioid receptor agonist which means it reduces sympathetic nervous system tone, and causes respiratory depression and analgesia. Remifentanil is an Opioid Agonist. The mechanism of action of remifentanil is as a Full Opioid Agonist.

MECHANISM OF ACTION:

Remifentanil is a new synthetic opioid with direct action on mu-opioid receptors. It has a rapid onset and short latency to peak effect. It is rapidly inactivated by esterases in both blood and tissues, resulting in a very short duration of action.

ADVERSE EFFECT:

- Fast or slow heart rate
- Stiff muscles
- Low blood pressure
- Blurred vision
- Difficult or troubled breathing
- Lightheadedness
- Pale or blue lips, fingernails, or skin.
- Unusual tiredness or weakness.

DOSES:

Powder for injection:
1mg/vial
2mg/vial
5mg/vial

MIXED AGONIST - ANTAGONIST:

In pharmacology the term agonist-antagonist or mixed agonist/antagonist is used to refer to a drug which under some conditions behaves as an agonist (a substance that fully activates the receptor that it binds to) while under other conditions, behaves as an antagonist (a substance that binds to a receptor but does not activate and can block the activity of other agonists).

1. BUPRENORPHINE:

Buprenorphine is an opioid partial agonist. It is used in medication-assisted treatment (MAT) to help people reduce or quit their use of heroin or other opiates, such as pain relievers like morphine.

At analgesic doses, buprenorphine is 20-50 times more potent than morphine. Because of its low intrinsic activity at the mu receptor, however, at increasing doses, unlike a full opioid agonist, the agonist effects

of buprenorphine reach a maximum and do not continue to increase linearly with increasing doses of the drug-the ceiling effect. One consequence of the ceiling effect is that an overdose of buprenorphine is less likely to cause fatal respiratory depression than is an overdose of a full mu opioid agonist.

It has sufficient agonist properties such that individuals addicted to opioids perceive a reinforcing subjective effect from the medication, often described in terms of “feeling normal.”

Buprenorphine has unique pharmacological properties that help:

- Lower the potential for misuse
- Diminish the effects of physical dependency to opioids, such as withdrawal symptoms and cravings
- Increase safety in cases of overdose

2. PENTAZOCINE:

Pentazocine is a synthetic opioid that has both partial agonist and antagonist activity and is similar to butorphanol. Pentazocine has weak antagonist or partial agonist activity to the μ type opiate receptors, with full agonist activity at the κ opioid receptor. These actions lead to typical analgesic effects of the opioids at low doses, but with a dysphoric effect at higher doses, which is believed to limit its abuse potential and puts a ceiling on its analgesic effect.
Pentazocine causes similar respiratory depression to that seen with equipotent doses of morphine and meperidine, but it exhibits a ceiling effect with doses in excess of 60 mg. Psychomimetic effects (e.g., dysphoria, hallucinations) may complicate its use, particularly with increasing doses.

3. NALBUPHINE

Nalbuphine, sold under the brand names Nubain among others, is a semisynthetic mixed agonist/antagonist opioid modulator which is used in the treatment of pain. It is given by injection into a vein, muscle, or fat.

Nalbuphine is said to be more morphine-like at lower doses. However at higher doses, it produces more sedation, drunkenness, dysphoria, and dissociation. As such, its effects are dose-dependent. Such effects include sedation majorly, dizziness or vertigo, lightheadedness, anxiety, dysphoria, euphoria, confusion, hallucinations, depersonalization, unusual dreams and feelings of "unreality"

Nalbuphine is a potent analgesic. Its analgesic potency is essentially equivalent to that of morphine on a milligram basis, which is based on relative potency studies using intramuscular administration. The elimination half-life of nalbuphine is approximately 5 hours.

OPIOID ANTAGONIST:

NALOXONE

A synthetic potent antagonist of narcotic drugs (such as morphine and fentanyl) that is administered especially in the form of its hydrochloride $C_{19}H_{21}NO_4 \cdot HCl$

NOTE: Naloxone is administered by injection or as a nasal spray to reverse the effects of opioids especially in the emergency treatment of opioid overdose. It is also administered in combination with buprenorphine in the form of a dissolvable tablet placed under the tongue or a film placed inside the cheek to treat opioid dependence.

MECHANISM OF ACTION

Naloxone is a competitive inhibitor of the μ-opioid receptor. Naloxone antagonizes the action of opioids, reversing their effects. If a patient has not taken opioids, naloxone does not have a significant effect on patients.

USES:

1-Emergency treatment

This medication is used for the emergency treatment of known or suspected opioid overdose. Serious overdose symptoms may include unusual sleepiness, unusual difficulty waking up, or breathing problems (ranging from slow/shallow breathing to no breathing).

2-In Low Blood Pressure

Other symptoms of overdose may include very small "pinpoint" pupils, slow heartbeat, or low blood pressure. If someone has serious overdose symptoms but you are not sure if the symptoms are due to overdose, give this medication right away anyway, since lasting slow/shallow breathing may cause permanent damage to the brain or death.

3-Opoid Antagonists

This medication belongs to a class of drugs known as opioid antagonists. It works by blocking the effects of the opioid in the brain. This medication may not work as well to block the effects of certain types of opioids (mixed agonist/antagonists such as buprenorphine, pentazocine). With these types of opioids, blocking may be incomplete or you may need a higher dose of naloxone.The effects of naloxone will not last as long as the effects of the opioid. Since treatment with this medication is not long-lasting, be sure to get medical help right away after giving the first dose of naloxone. Treatment of opioid overdose should also

include breathing treatment (such as oxygen given through tubes in the nose, mechanical ventilation, artificial respiration).

SIDE EFFECTS:

1-Sweating: In someone who has been using an opioid regularly, withdrawal symptoms can happen suddenly after receiving this medication. Withdrawal symptoms may include body aches, fever, sweating.

2-Weakness

Patient may also feel runny nose, sneezing, goose bumps, yawning, weakness, shivering/trembling, nervousness, restlessness, diarrhea, nausea/vomiting, stomach cramps, increased blood pressure, fast heartbeat.

3-Harmful for Infants: In babies younger than 4 weeks who have been receiving an opioid regularly, sudden opioid withdrawal may be life-threatening if not treated the right way. Symptoms in babies may include seizures, crying more than usual, and muscle twitching/spasms.

DOSES:

The manufacturer recommended initial dose is **2 mg or 4 mg IN or 0.4 mg or 2 mg IM/SC** to be repeated after 2–3 min if needed; however, there is no consensus nor recommendation to guide which of the available doses should be selected in a given case of opioid overdose.

NALTREXONE

Naltrexone, sold under the brand name **Revia** among others, is a medication primarily used to manage alcohol or opioid use disorder by reducing cravings and feelings of euphoria associated with substance use disorder. It has also been found to be effective in the treatment of other addictions and may be used for them off-label. An opioid-dependent person should not receive naltrexone before detoxification. It is taken by mouth or by injection into a muscle. Effects begin within 30 minutes. A decreased desire for opioids may take a few weeks to occur.

MECHANISM OF ACTION:

Naltrexone is a pure opiate antagonist and has little or no agonist activity. The mechanism of action of naltrexone in alcoholism is not understood; however, involvement of the endogenous opioid system is suggested by preclinical data. Naltrexone is thought to act as a competitive antagonist at mc, κ, and δ receptors in the CNS, with the highest affintiy for the μ receptor. Naltrexone competitively binds to such receptors and may block the effects of endogenous opioids. This leads to the antagonization of most of the subjective and objective effects of opiates, including respiratory depression, miosis, euphoria, and

drug craving. The major metabolite of naltrexone, 6-β-naltrexol, is also an opiate antagonist and may contribute to the antagonistic activity of the drug.

USES:

1-Prevention for drug addicted person

This medication is used to prevent people who have been addicted to certain drugs (opiates) from taking them again. It is used as part of a complete treatment program for drug abuse (such as compliance monitoring, counseling, behavioral contract, lifestyle changes). This medication must not be used in people currently taking opiates, including methadone. Doing so can cause sudden withdrawal symptoms.

2-Opiate antagonists

Naltrexone belongs to a class of drugs known as opiate antagonists. It works in the brain to prevent opiate effects (such as feelings of well-being, pain relief). It also decreases the desire to take opiates.Ask your doctor or pharmacist if you should have naloxone available to treat opioid overdose. Teach your family or household members about the signs of an opioid overdose and how to treat it.

3-Cure for Alcohol addiction: This medication is also used to treat alcohol abuse. It can help people drink less alcohol or stop drinking altogether. It also decreases the desire to drink alcohol when used with a treatment program that includes counseling, support, and lifestyle changes.

SIDE EFFECTS:

1-Anxiety

Nausea, headache, dizziness, anxiety, tiredness, and trouble sleeping may occur. In a small number of people, mild opiate withdrawal symptoms may occur, including abdominal cramps, restlessness, bone/joint pain, muscle aches, and runny nose. If any of these effects last or get worse, tell your doctor or pharmacist promptly.

2-Abdominal issues

Sudden opiate withdrawal symptoms can occur within minutes after taking naltrexone. Tell your doctor right away if any of these withdrawal symptoms occur: abdominal cramps, nausea/vomiting, diarrhea, joint/bone/muscle aches, mental/mood changes (such as anxiety, confusion, extreme sleepiness, visual hallucinations), runny nose.

3-Liver disease

Naltrexone has rarely caused serious liver disease. The risk is increased when larger doses are used. Discuss the risks and benefits with your doctor. Stop using this medication and tell your doctor right away if you develop symptoms of liver disease, including: nausea/vomiting that doesn't stop, severe stomach/abdominal pain, dark urine, yellowing eyes/skin.

4-Allergic reactions

A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction, including: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.