

Methadone

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Methadone is a potent synthetic opiate. It is primarily used in the treatment of moderate to severe pain (Dolmed® 5mg tablets) and also in opioid replacement therapy (Methadone Martindale Pharma® 2 mg/ml solution and others). Like other opiates, methadone is both mentally and physically addictive.

Methadone continues to be used across the world as an analgesic. The first scientific evidence of its suitability for the treatment of heroin addiction was published in 1965. Methadone is the most commonly used opioid replacement therapy (ORT) in Europe. In Finland, 40% of all ORT patients, a total of some 700 individuals, are prescribed methadone. Current estimates suggest that there are some 4,000 to 6,000 recreational opiate users in Finland, many of whom are mixed users. No detailed data are available on methadone abuse specifically.

Mechanism of action

Methadone affects the central nervous system and is a μ -opioid receptor agonist. Methadone inhibits the reuptake of both serotonin and noradrenalin, which is responsible for its analgesic effect.

Methadone is effectively absorbed orally, although exact rates are subject to significant individual variation. Onset occurs after 30-60 minutes. Following a single oral dose, effects may last for approximately 4 hours but individual susceptibility varies greatly. With continued administration the effects tend to be longer, as it persists in tissue: when used for ORT purposes, methadone is administered once daily. The half-life of methadone is approximately 24 hours. When consumed orally, methadone has a bitter flavour.

Effects and side effects

For patients who have not previously used opiates, the effects of methadone are similar to morphine. Methadone is a central nervous system depressant and can cause drowsiness and feelings of well being often sought by recreational users. Common side effects include nausea, vomiting and constipation as well as anorexia or lack of appetite, dry mouth, sweating and tiredness. It is also associated with loss of libido, hypotension, ECG changes and muscle twitching. In addition to drowsiness, methadone can also cause respiratory depression, which is one of the most severe side effects. Due to the changes to the serotonin reuptake process, methadone increases the risk of so-called serotonin syndrome.

In long-term use, the body gets used to methadone and the user requires increasingly large doses to achieve the desired effect. With a few exceptions, including constipation and miosis, the body will also adjust to the majority of the side effects of methadone. In prolonged use, methadone no longer causes the previous sense of well-being and mainly suppresses the appearance of side effects.

Withdrawal symptoms

Users who abruptly stop their methadone intake often experience withdrawal symptoms (see Table 1). Due to its long half-life, the side effects are often milder than those associated with short-acting opiates but they are longer lasting. They are characterised by a delayed onset, peaking four to six days after discontinuation. The symptoms usually persist between 10 to 12 days but can continue for longer. The symptoms are rarely life-threatening.

Table 1. Most common opiate withdrawal symptoms.

Symptoms:
Yawning, weakness, depression, diarrhoea, nausea
Sweating, increased saliva production, tearfulness, strong nasal congestion, sneezing
Muscle aches, internal organ pain, intestinal spasms, vomiting
Restlessness, difficulty sleeping, anxiety, tremors, relapses
Anorexia, weight loss, pupillary dilation, increased heart rate, goose bumps

Pyrexia (fever), hypertension, increased respiratory rate, feeling cold

Misuse and overdose

In long-term use, methadone's capacity for generating a feeling of well-being is reduced. However, in intravenous use this effect is retained to a certain extent. Lower doses are also required for intravenous use. This is why recreational users often inject methadone. Intravenous use is more addictive. As a long-acting opiate, methadone is particularly hazardous when used intravenously. However, the risks associated with oral use should not be understated either.

The doses prescribed for ORT are lethal for occasional users and even experienced users, particularly if there has been a temporary break in their consumption. A lethal dose for methadone-naïve users is estimated at 50-100mg. The dose is lower if administered intravenously. In ORT, initial daily doses start at 10-40mg, rising to 60-120mg for maintenance treatment. If a patient omits several maintenance treatment doses, the next dose will need to be reduced by 25 to 50% to account for the reduced tolerance. When the ORT is discontinued, the dosage is reduced gradually, commonly by 2.5 to 5 mg per week.

As methadone preparations, including tablets and solutions, are not intended for intravenous administration, those who inject will also introduce a number of additives to their circulatory system, which may block blood vessels and cause inflammation and damage to the eyes.

A methadone overdose can be treated with naloxone administered parenterally. As methadone is a long-acting agent, repeated doses may be required until the effects have completely worn off. The number of deaths associated with methadone has grown steadily in the 2000s. They are often due to concomitant use of methadone and other drugs, particularly benzodiazepine, alcohol and other opiates.

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