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(54) Title: BUPRENOPHINE-WAFER FOR DRUG SUBSTITUTION THERAPY

(57) Abstract: The present invention relates to oral pharmaceutical dosage forms comprising buprenorphine with the dosage form releasing buprenorphine instantly upon oral, preferably sublingual, application of the dosage form. The present invention also relates to the use of such dosage forms for treating pain in a human or animal or for drug substitution therapy in drug- dependent human subjects.

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BUPRENORPHINE-WAFER FOR DRUG SUBSTITUTION THERAPY

The present invention relates to oral pharmaceutical dosage forms comprising buprenorphine with the dosage form releasing buprenorphine instantly upon oral, preferably sublingual, application of the dosage form. The present invention also relates to the use of such dosage forms for treating pain in a human or animal or for drug substitution therapy in drug-dependent human subjects.

Background of the Invention

Chronic pain, which may be due to idiopathic reasons, cancer or other diseases such as rheumatism and arthritis, is typically treated with strong opioids.

Over the last decades prejudices in the medical community as to the use of strong opioids for treating chronic pain in patients has significantly decreased. Many of these prejudices were due to some of the characteristics being inherent to opioids.

While opioids have always been known to be useful in pain treatment, they also display an addictive potential in view of their euphorigenic activity. Thus, if opioids are taken by healthy human subjects with a drug seeking behaviour they may lead to psychological as well as physical dependence.

These usually undesired characteristics of opioids can however become important in certain scenarios such as drug substitution therapies for drug addicts. One of the fundamental problems of illicit drug abuse by drug addicts ("junkies") who are dependent on the constant intake of illegal drugs such as heroin is the drug-related criminal activities resorted to by such addicts in order to raise enough money to fund their addiction. The constant pressures upon addicts to procure money for buying drugs and the concomitant criminal activities have been increasingly recognised as a major factor that counteracts efficient and long-lasting withdrawal and abstinence from drugs.

Therefore, programmes have been developed, particularly in the United States and western European countries, in which drug addicts are allowed to take prescription drugs under close supervision of medical practitioners instead of illegal drugs such as street heroin.

The aim of drug substitution theory is thus to first enable addicts to lead a regular life by administering legal drugs to prevent withdrawal symptoms, but because of their legal character and prescription by medical practitioners do not lead to the aforementioned described drug-related criminal activities. In a second and / or alternate step in the treatment of drug addiction may be to slowly make the drug addict less dependent on the drug by gradually reducing the dose of the substitution drug or to bridge the time until a therapy place in a withdrawal programme is available.

The standard drug used in drug substitution therapy programmes has for a long time been methadone. However, in recent years the potential of other opioids as substitution drugs in substitution therapy has been recognised. A particularly suitable drug for that purpose is the opioid buprenorphine, which is a mixed opioid agonist/antagonist.

Nowadays, buprenorphine preparations are administered in drug substitution programmes in the form of a tablet for sublingual administration. One of the reasons that the tablets are

formulated for sublingual administration is that this the preferred route of administration for buprenorphine. Furthermore, if a patient swallows such tablets they will not provide euphorigenic activity.

One example of sublingual tablets for drug substitution therapy is the preparation Subutex® (being marketed in Germany by Essex Pharma).

Nevertheless, drug addicts sometimes still try to divert these sublingual buprenorphine tablets by removing them from the mouth when the supervising healthcare professional's attention is directed to other activities. Later the tablets may be sold or the active agent buprenorphine isolated/extracted to apply it parenterally.

Another buprenorphine preparation aimed at preventing this potential possibility of abuse has recently gained administrative approval in the United States (Suboxone®). The Suboxone® preparation comprises buprenorphine hydrochloride and the opioid antagonist naloxone hydrochloride dihydrate. The presence of naloxone is intended to prevent parenteral abuse of buprenorphine as parenteral co-administration of buprenorphine and naloxone in e.g. an opioid-dependent addict will lead to serious withdrawal symptoms.

However, there remains a need for other diversion and / or abuse-resistant dosage forms of buprenorphine, which can be used in drug substitution therapy as described above. Additionally, it would be desirable to have a buprenorphine preparation available which is diversion and / or abuse-resistant in cases where the preparation is used for drug substitution therapy and which could also provide efficient analgesia in cases where the preparation is administered to alleviate pain in a patient.

Object and Summary of the Invention

It is an object of the present invention to provide an oral pharmaceutical dosage form of the active agent buprenorphine that is less prone to diversion and / or abuse in drug substitution therapy. It is another object of the present invention to provide an oral dosage form of the active agent buprenorphine that can be used for drug substitution therapy and/or pain treatment.

In one embodiment the present invention relates to an oral pharmaceutical dosage form comprising at least buprenorphine or a pharmaceutically acceptable salt thereof with a dosage form releasing buprenorphine or said pharmaceutically acceptable salt thereof instantly upon or oral, preferably sublingual, application of the dosage form. It is, however, understood that the invention and its various embodiments which are set out below, can be extended to any opioid or analgesic whose preferred route of administration is oral, prefereably sublingual, as is the case for buprenorphine.

An instant release of buprenorphine or a pharmaceutically acceptable salt thereof upon oral, preferably sublingual, application means that substantially all of the buprenorphine or said pharmaceutically acceptable salt thereof will be released within less than three minutes, preferably within less than two minutes or less than one minute. Even more preferably, substantially all of the buprenorphine or said pharmaceutically acceptable salt thereof will be released within less than thirty seconds, twenty seconds, ten seconds or even within less than five seconds after oral, preferably sublingual, application of the dosage form. In one of the preferred embodiments these oral dosage forms will comprise between approximately 0.1 mg and approximately 16 mg buprenorphine or the equivalent amounts of a pharmaceutically acceptable salt thereof.

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