of increasing the dosage due to tolerance effects thereby promoting vascular irritation and overshoot reactions.

BRIEF DESCRIPTION ~~OF THE INVENTION~~

The object of the disclosure~~invention~~ is solved by the present disclosure~~invention~~.
The present disclosure provides in one aspect a formulation of landiolol hydrochloride for persistent reduction of the heart rate and/or blood pressure during the administration period of landiolol hydrochloride in the treatment of a human suffering from tachycardia, tachyarrhythmia and/or hypertension , wherein landiolol hydrochloride is administered at a constant dose of more than 5 µg/kg/min for a period of at least 2 hours.
The ~~invention~~ disclosure provides a formulation of landiolol hydrochloride in a therapeutically efficient amount for use in the treatment of a subject suffering from tachycardia, tachyarrhythmia and/or hypertension, wherein landiolol hydrochloride is administered at a constant dose of about 5 µg/kg/min, specifically more than (>) 5 µg/kg/min, preferably at least 10 µg/kg/min for a period of at least 2 hours, preferably for at least 4 hours, preferably for at least 6 hours, preferably for at least 12 hours, preferably for at least 20 hours, preferably for at least 24 hours, preferably for at least 2 days, preferably for more than two days and wherein the heart rate and/or blood pressure of said patient are persistently reduced during the administration period compared to the heart rate and/or blood pressure before treatment, specifically as opposed to other short acting beta blocker such as esmolol.
According to a further embodiment of the disclosure~~invention~~, the constant dose of landiolol hydrochloride is at least 15 µg/kg/min, specifically at least 20 µg/kg/min, specifically at least 25 µg/kg/min, specifically at least 30 µg/kg/min, specifically at least 35 µg/kg/min, specifically at least 40 µg/kg/min.
According to a further embodiment of the disclosure~~invention~~ the heart rate and/or blood pressure are reduced at least 5%, preferably between 10% and 50% compared to the heart rate and/or blood pressure before treatment with landiolol.
Overshoot is not occurring after termination of administration and normal heart rate and/or blood pressure are attained within a few minutes, specifically within 5 to 20 minutes and more specifically, said normal heart rate and/or blood pressure are preserved for at least 30 minutes, preferably for at least 60 minutes, more preferred at least 120 minutes after termination of administration of landiolol-hydrochloride as opposed to esmolol where an overshoot occurs within minutes and may be maintained hours thus leading to increased heart rate and/or blood pressure.

According to the disclosure~~invention~~, the formulation thus shows a reduced or no overshoot effect with regard to the heart rate and/or blood pressure after termination of administration.

According to an embodiment of the disclosure~~invention~~, landiolol-hydrochloride is at a concentration of about 1 to 30 mg/mL, preferably about 5 to 15 mg/mL.

According to the embodiment of the disclosure~~invention~~, the administration of a pharmaceutical composition comprising landiolol-hydrochloride for the use according of the present invention, may be done in a variety of ways, including orally, subcutaneously, intravenously, intraarterially, intracoronary, intranasally, intraotically, transdermally, mucosally, topically, e.g., gels, salves, lotions, creams, etc., intraperitoneally, intramuscularly, intrapulmonary, e.g. employing inhalable technology or pulmonary delivery systems, vaginally, parenterally, rectally, or intraocularly.

A specific embodiment provides a formulation wherein landiolol hydrochloride is a lyophilized powder reconstituted to obtain a ready to use i.v. solution, optionally the i.v. solution has a pH of up to 6.5 and as a further option, said i.v. solution is administered as continuous infusion.

According to an embodiment, said i.v. solution is administered as maintenance infusion at a dose of between 5 to 100 µg/kg/min, preferably 10 to 100 µg/kg/min, preferably between 10 to 50 µg/kg/min.

In an embodiment, the i.v. solution is local tissue tolerant at the infusion site, preventing local venous irritation or skin necrosis at the infusion site.

In a specific embodiment, the subject is suffering from supraventricular tachycardia.

In a further specific embodiment, the subject is suffering from hypertension, specifically from primary or secondary hypertension or hypertensive crisis.

The inventive use is specifically for treating a subject, wherein said subject is

a. suffering from tachycardia selected from, supraventricular tachycardia, ventricular tachycardia, hypertension and non-compensatory sinus tachycardia, atrial tachycardic fibrillation, atrial flutter in perioperative, postoperative, or other circumstances where persistent control of the ventricular rate is desirable, or