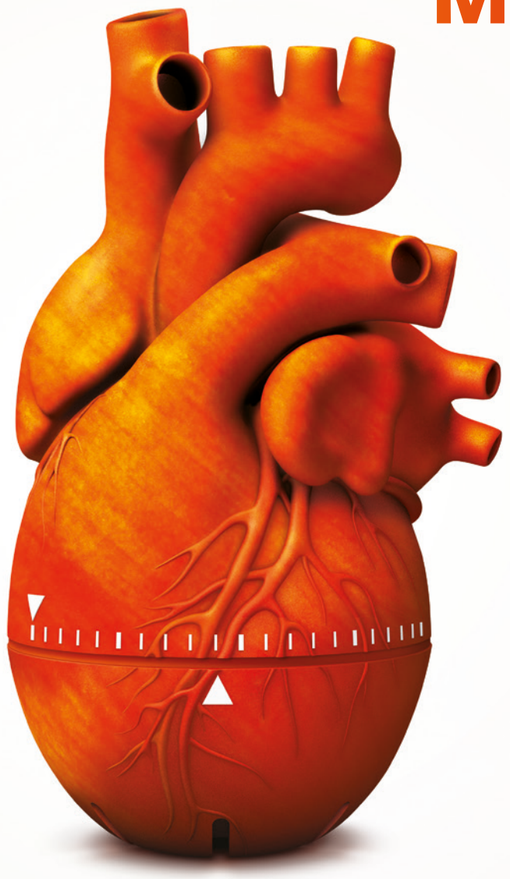
GIVES YOU TIME WHEN IT'S NEEDED MOST



SIMDAX®
levosimendan

EASE THE CHALLENGE OF TREATING THE FAILING HEART

06/2018

PRODUCT INFORMATION:
Simdax 2.5 mg/ml concentrate for solution for infusion.

Therapeutic indications
Simdax is indicated for the short-term treatment of acutely decompensated severe chronic heart failure (ADHF) in situations where conventional therapy is not sufficient, and in cases where inotropic support is considered appropriate.

Dosage and administration
Simdax is for in-hospital use only. It should be administered in a hospital setting where adequate monitoring facilities and expertise with the use of inotropic agents are available.

Simdax is to be diluted prior to administration. The infusion is for intravenous use only and can be administered by the peripheral or central route.

Dosage: The dose and duration of treatment should be individualised according to the patient's clinical condition and response.

The recommended duration of infusion in patients with acute decompensation of severe chronic heart failure is 24 hours. No signs of development of tolerance or rebound phenomena have been observed following discontinuation of Simdax infusion. Haemodynamic effects persist for at least 24 hours and may be seen up to 9 days after discontinuation of a 24-hour infusion.

Experience of repeated administration of Simdax is limited. Experience with concomitant use of vasoactive agents, including inotropic agents (except digoxin) is limited.

Monitoring of treatment: Consistent with current medical practice, ECG, blood pressure and heart rate must be monitored during treatment and the urine output measured. Monitoring of these parameters for at least 3 days after the end of infusion or until the patient is clinically stable is recommended. In patients with mild to moderate renal or mild to moderate hepatic impairment monitoring is recommended for at least 5 days.

Elderly: No dose adjustment is required for elderly patients.

Renal impairment: Simdax must be used with caution in patients with mild to moderate renal impairment. Simdax should not be used in patients with severe renal impairment (creatinine clearance <30 ml/min).

Hepatic impairment: Simdax must be used with caution in patients with mild to moderate hepatic impairment although no dose adjustment appears necessary for these patients. Simdax should not be used in patients with severe hepatic impairment.

Children: Simdax should not be administered to children and adolescents under 18 years of age.

Contraindications
Hypersensitivity to levosimendan or to any of the excipients. Severe hypotension and tachycardia. Significant mechanical obstructions affecting ventricular filling or outflow or both. Severe renal impairment (creatinine clearance <30 ml/min) and severe hepatic impairment. History of Torsades de Pointes.

Special warnings and special precautions for use
An initial haemodynamic effect of levosimendan may be a decrease in systolic and diastolic blood pressure, therefore, levosimendan should be used with caution in patients with low baseline systolic or diastolic blood pressure or those at risk for a hypotensive episode. More conservative dosing regimens are recommended for these patients. Physicians should tailor the dose and duration of therapy to the condition and response of the patient.

Severe hypovolaemia should be corrected prior to levosimendan infusion. If excessive changes in blood pressure or heart rate are observed, the rate of infusion should be reduced or the infusion discontinued.

The exact duration of all haemodynamic effects has not been determined, however, the haemodynamic effects, generally last for 7-10 days. This is partly due to the presence of active metabolites, which reach their maximum plasma concentrations about 48 hours after the infusion has been stopped. Non-invasive monitoring for at least 4-5 days after the end of infusion is recommended. Monitoring is recommended to continue until the blood pressure reduction has reached its maximum and the blood pressure starts to increase again, and may need to be longer than 5 days if there are any signs of continuing blood pressure decrease, but can be shorter than 5 days if the patient is clinically stable. In patients with mild to moderate renal or mild to moderate hepatic impairment an extended period of monitoring maybe needed.

Simdax infusion should be used cautiously in patients with tachycardia atrial fibrillation with rapid ventricular response or potentially life-threatening arrhythmias.

Interaction with other medicinal products and other forms of interaction
Consistent with current medical practice, levosimendan should be used with caution when used with other intravenous vasoactive medicinal products due to a potentially increased risk of hypotension.

No pharmacokinetic interactions have been observed in a population analysis of patients receiving digoxin and Simdax infusion. Simdax infusion can be used in patients receiving beta-blocking agents without loss of efficacy. Co-administration of isosorbide mononitrate and levosimendan in healthy volunteers resulted in significant potentiation of the orthostatic hypotensive response.

Undesirable effects
The most commonly (>1/10) reported adverse reactions include headache, hypotension and ventricular tachycardia.

Overdose
Overdose of Simdax may induce hypotension and tachycardia. High doses (at or above 0.4 microgram/kg/min) and infusions over 24 hours increase the heart rate and are sometimes associated with prolongation of the QTc interval. Simdax overdose leads to increased plasma concentrations of the active metabolite, which may lead to a more pronounced and prolonged effect on heart rate requiring a corresponding extension of the observation period.

Storage
Store at 2°C-8°C (in a refrigerator). Do not freeze.

CONTACT INFORMATION:
Orion Corporation, Orion Pharma, PO Box 65, FI-02101 ESPOO, FINLAND. Tel. +358 10 4261

ORION PHARMA
Building well-being

SIMDAX®
levosimendan

WELCOME TO THE PRACTICAL TUTORIALS ON INODILATION IN ACUTE AND ADVANCED HEART FAILURE

on August 26 – 28 at the ESC 2018

The use of inotropes for correcting hemodynamic dysfunction in patients with congestive heart failure has been described over many decades.

However, negative or insufficient data has been collected on the effects of cardiac glycosides, cathecolamines, and phosphodiesthrase inhibitors on quality of life and survival.

More recently, the calcium sensitizer and potassium channel opener levosimendan has been proposed as a safer inodilator.[1]

This series of tutorials focus on how to use safely and effectively levosimendan in acute and advanced heart failure.

Ref. 1. Pollesello P et al. Int J Cardiol. 2016;203:543-8

ORION PHARMA
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SUN, 26 AUGUST 2018

Sunday, 26 August 10:00 – 11:00 Practical Tutorials 6

Inotropes in Acute Heart Failure: from guidelines to practical use

10:00 – 10:30 Guidelines and patient characteristics
Alexandre Mebazaa – Paris, France

10:30 – 11:00 Therapeutic options and clinical practice
John Parissis – Athens, Greece

Sunday, 26 August 11:30 – 12:30 Practical Tutorials 6

Acute Heart Failure related to acute coronary syndromes: is there a role for inodilators?

11:30 – 12:00 Patient characteristics
Veli-Pekka Harjola – Helsinki, Finland

12:00 – 12:30 Therapeutic options and clinical practice
Carsten Tschöpe – Berlin, Germany

Sunday, 26 August 13:00 – 14:00 Practical Tutorials 6

Inodilators and renal function: how to avoid kidney dysfunction in Acute Heart Failure?

13:00 – 13:30 Cardio-renal syndrome
Finn Gustafsson – Copenhagen, Denmark

13:30 – 14:00 Therapeutic options and clinical practice
Simon Matskeplishvili – Moscow, Russia

Sunday, 26 August 14:30 – 15:30 Practical Tutorials 6

Inotropes or inodilators in HFrEF: what to use, on whom, when and how?

14:30 – 15:00 What is available?
Zoltan Papp – Debrecen, Hungary

15:00 – 15:30 Therapeutic options and clinical practice
Attila Borbely – Debrecen, Hungary

Sunday, 26 August 16:00 – 17:00 Practical Tutorials 6

Repetitive use of inodilators in Advanced Heart Failure

16:00 – 16:30 Patient characteristics
Francesco Fedele – Rome, Italy

16:30 – 17:00 Therapeutic options and clinical practice
Fabrizio Oliva – Milan, Italy

Refreshments will be served at each session.

MON, 27 AUGUST 2018

Monday, 27 August 10:00 – 11:00 Practical Tutorials 6

Inotropes in Acute Heart Failure: from guidelines to practical use

10:00 – 10:30 Guidelines and patient characteristics
Friedrich Fruhwald – Graz, Austria

10:30 – 11:00 Therapeutic options and clinical practice
Dirk von Lewinski – Graz, Austria

Monday, 27 August 11:30 – 12:30 Practical Tutorials 6

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15:00 – 15:30 Therapeutic options and clinical practice
Robert H Schwinger – Weiden, Germany

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16:00 – 16:30 Patient characteristics
Josep Comin-Colet – Barcelona, Spain

16:30 – 17:00 Therapeutic options and clinical practice
Gerhard Pölzl – Innsbruck, Austria

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TUE, 28 AUGUST 2018

Tuesday, 28 August 10:00 – 11:00 Practical Tutorials 6

Inotropes in Acute Heart Failure: from guidelines to practical use

10:00 – 10:30 Guidelines and patient characteristics
Friedrich Fruhwald – Graz, Austria

10:30 – 11:00 Therapeutic options and clinical practice
Dirk von Lewinski – Graz, Austria

Tuesday, 28 August 11:30 – 12:30 Practical Tutorials 6

Acute Heart Failure related to acute coronary syndromes: is there a role for inodilators?

11:30 – 12:00 Patient characteristics
Matti Kivikko – Espoo, Finland

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John Parissis – Athens, Greece

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