Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nitro-Dur 0.1 mg/hr Transdermal Patch

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Content of the active substance per patch: Glyceryl trinitrate 37.4 % w/w (20 mg).
Dose delivered per unit time: 0.1 mg/hr.
Area of the releasing surface: 5cm^2

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Transdermal Patch.
Round patch with one side consisting of tan-coloured Saranex 2014 extruded film with the name Nitro-Dur, the dosage for one hour and the area of the patch.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For prophylaxis of angina pectoris.

4.2 Posology and method of administration

Adults, including elderly patients:
The recommended initial dose is one 0.2mg/h Nitro-Dur patch daily. In some patients dose titration to higher or lower doses may be necessary to achieve optimum therapeutic effect.

Nitro-Dur is suitable for continuous or intermittent use. Patients already receiving continuous 24-hour nitrate therapy without signs of nitrate tolerance may continue on this regimen provided clinical response is maintained. Attenuation of effect has however occurred in some patients being treated with sustained release nitrate preparations. In such patients intermittent therapy may be more appropriate. Under these circumstances Nitro-Dur is applied daily for a period of approximately 12 hours. The patch is then removed to provide a nitrate-free interval of 12 hours which may be varied between 8-12 hours to suit individual patients.

Maximum dose : 15 mg in 24 hours.

Patients experiencing nocturnal angina may benefit from overnight treatment with a nitrate-free interval during the day. In this patient group additional anti-anginal therapy may be needed during the day.

Patients with severe angina may need additional anti-anginal therapy during nitrate-free intervals.

Nitro-Dur Transdermal patches may be applied to any convenient skin area; the recommended site is the chest or outer upper arm. Application sites should be rotated and suitable areas may be shaved if necessary. Nitro-Dur patches should not be applied to the distal part of the extremities.

Children :
Not recommended.

4.3 Contraindications

Contra-indicated in patients hypersensitive to nitrates and in patients with marked anaemia. Use is also contra-indicated in severe hypotension, increased cranial pressure, cerebral haemorrhage, head trauma and myocardial insufficiency due to valvular or left ventricular outflow tract obstruction, hypertrophic obstructive cardiomyopathy, cardiac tamponade, constrictive pericarditis as well as closed-angle glaucoma..

Phosphodiesterase inhibitors, e.g. sildenafil, tadalafil, vardenafil have been shown to potentiate the hypotensive effects of nitrates and their co−administration with nitrates or nitric oxide donors is therefore contra-indicated.

4.4 Special warnings and precautions for use

Nitro-Dur should only be used under careful clinical and/or haemodynamic monitoring in patients with acute myocardial infarction or congestive heart failure. Nitro-Dur is not indicated for the immediate treatment of acute anginal attacks.

As with all anti-anginal nitrate preparations, withdrawal of treatment should be gradual, by replacement with decreasing doses of long-acting oral nitrates.

Nitro-Dur should be removed before attempting defibrillation or cardioversion, to avoid possibility of electrical arcing, and before diathermy.

The possibility of increased frequency of angina during patch-off periods should be considered. In such cases, the use of concomitant anti-anginal therapy is desirable.

In some patients severe hypotension may occur particularly with upright posture, even with small doses of glyceryl trinitrate. Thus Nitro-Dur should be used with caution in patients who may have volume depletion from diuretic therapy and in patients who have low systolic blood pressure (e.g. below 90mm Hg).

Paradoxical bradycardia and increased angina may accompany glyceryl-trinitrate-induced hypotension.

Caution should be exercised in patients with arterial hypoxaemia, due to severe anaemia and patients with hypoxaemia and a ventilation/perfusion imbalance due to lung disease or ischaemic heart failure, where biotransformation of GTN may be reduced.

Nitrate therapy may aggravate the angina caused by hypertrophic cardiomyopathy.

This product should be used with extreme caution in patients pre-disposed to closed angle glaucoma.

The lowest effect dose should be used

Attenuation of effect has occurred in some patients being treated with sustained release preparations. In such patients intermittent therapy may be more appropriate (see section 4.2).

Caution should be exercised in patients suffering from hypothyroidism, malnutrition, severe renal or hepatic impairment, hypothermia and recent history of myocardial infarction.

Severe postural hypotension with light-headedness and dizziness is frequently observed after the consumption of alcohol.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with other vasodilators, calcium antagonists, ACE inhibitors, beta-blockers, diuretics, antihypertensives, tricyclic antidepressants and major tranquillisers, as well as the consumption of alcohol, may potentiate the blood pressure lowering effects of Nitro-Dur.

Concurrent administration of Nitro-Dur with dihydroergotamine may increase the bioavailability of dihydroergotamine and lead to coronary vasoconstriction.

The possibility that the ingestion of acetyl salicylic acid and non-steroidal anti-inflammatory drugs might diminish the therapeutic response to Nitro-Dur cannot be excluded.

The hypotensive effects of nitrates are potentiated by concurrent administration of phosphodiesterase inhibitors, e.g. sildenafil, tadalafil, vardenafil. (see section 4.3).

4.6 Fertility, pregnancy and lactation

Nitro-Dur should not be prescribed during pregnancy or for women breast feeding infants unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

Nitrates may cause dizziness and blurred vision, which may affect ability to drive and operate machines.

4.8 Undesirable effects

Headache is the most common side-effect, especially at higher doses. Transient episodes of dizziness and light-headedness which may be related to blood pressure change may also occur. Hypotension occurs infrequently but may be severe enough to warrant discontinuation of therapy. Syncope and reflex tachycardia have been reported but are uncommon. Application site reactions (including erythema, rash, burning and purpura) may occur but are rarely severe. Contact dermatitis has been reported. Hypersensitivity reactions may occur.

4.9 Overdose

High doses of glyceryl trinitrate may produce severe hypotension, syncope and methaemoglobinaemia. Increased intercranial pressure with associated cerebral symptoms may occur. Treatment is by removal of the patch or reduction of dose, depending on severity. Thorough scrubbing of underlying skin may reduce absorption more quickly after removal. Intravenous infusion of normal saline or similar fluid may be necessary to increase the central fluid volume. Any fall in blood pressure or signs of collapse that may occur may be managed by general supportive or resuscitative measures. Adrenaline and related products are ineffective in reversing the severe hypotensive events associated with overdose.

If methemoglobinemia is present, administration of methylene blue may be required.

Methemoglobinemia should be treated with methylene blue if the patient develops cardiac or CNS effects of hypoxia. The initial dose is 1-2 mg/kg infused intravenously over 5 minutes. The initial dose is 1 – 2 mg/kg infused intravenously over 5 minutes. Repeat methemoglobin levels should be obtained 30 minutes later and a repeat dose of 0.5 – 1.0 mg/kg may be used if the level remains elevated and the patient is still symptomatic. Relative contraindications for methylene blue include known NADH methemoglobin reductase or G-6-PD deficiency. Infants under the age of 4 months may not respond to methylene blue due to immature NADH methemoglobin reductase. Exchange transfusion has been used successfully in critically ill patients when methemoglobinemia is refractory to treatment

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vasodilators used in cardiac disease, ATC code : C01D A02.

Glyceryl trinitrate, (as other organic nitrates), is a potent dilator of vascular smooth muscle. The effect on veins predominates over that on arteries resulting in decreased cardiac preload. Systemic vascular resistance is relatively unaffected, heart rate is unchanged or slightly increased and pulmonary vascular resistance is consistently reduced.

5.2 Pharmacokinetic properties

Glyceryl trinitrate is rapidly hydrolysed by liver enzymes which are a major factor in bioavailability. Peak concentrations of glyceryl trinitrate following sub-lingual administration occur within 4 minutes in man with a half-life of 1 to 3 minutes. Transdermal delivery systems provide an alternative route to bypass the hepatic circulation with longer term gradual absorption providing prophylactic dosing. Steady state plasma concentrations of approximately 200 pg/ml are achieved within approximately 2 hours of application of Nitro-Dur and are maintained for 24 hours. Rate of absorption is controlled by the skin.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylacrylate Polymer (Polymer C)
Butylacrylate Polymer (Polymer D)
Sodium Polyacrylate (Polymer A)
Melamine Formaldehyde Resin (Polymer B)
Purified Water

Coated onto tan-coloured Saranex 2014 extruded thermoplastic film 5 cm^2. Adhesive layer covered by PVC Release Liner 5 cm^2.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate.

6.5 Nature and contents of container

Sealed pouches consisting of paper lined with polyethylene/foil laminate enclosing individual transdermal patches; 28 patches are contained in a cardboard carton.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Merck Sharp & Dohme Ireland (Human Health) Limited
Pelham House
South County Business Park
Leopardstown
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 1286/40/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 10 February 2007

10 DATE OF REVISION OF THE TEXT

November 2010