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Nitro-Dur 0.2mg/h; 0.4mg/h and 0.6mg/h Transdermal Patch

1. NAME OF THE MEDICINAL PRODUCT

Nitro-Dur 0.2mg/h; 0.4mg/h and 0.6mg/h Transdermal Patch

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Glyceryl trinitrate 37.4 % w/w

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Transdermal Patch

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For prophylaxis of angina pectoris either alone or in combination with other anti-anginal therapy.

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.

Maximum dose : 15 mg in 24 hours.

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 (see section 4.4).

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.

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.

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 use of Nitro-Dur with other vasodilating agents, alcohol, anti-hypertensive agents, beta-adrenergic blocking agents, ACE inhibitors, phenothiazines or calcium channel blocking agents may cause additive hypotensive effects.

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

4.6 Pregnancy and lactation

It is not known whether glyceryl trinitrate in transdermal form can affect reproductive capacity or cause foetal harm. Thus Nitro-Dur should only be administered to pregnant women if the potential benefit to the mother clearly outweighs the potential hazard to the foetus. It is not known whether glyceryl trinitrate is excreted in human milk. Caution should therefore be exercised when Nitro-Dur is administered to nursing mothers.

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 intracranial 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

In normal individuals or those with coronary artery disease (in the absence of heart failure) glyceryl trinitrate decreases cardiac output slightly. Doses which do not alter systemic arterial pressure often product arteriolar dilatation in the face and neck resulting in flushing. Dilatation of the meningeal arterioles may explain the headache which is often reported. Rapid administration of high doses of glyceryl trinitrate decreases blood pressure and cardiac output resulting in pallor, weakness, dizziness and activation of compensatory sympathetic reflexes. A marked hypotensive effect may occasionally occur especially in the upright position.

5.2 Pharmacokinetic properties

Glyceryl trinitrate is rapidly hydrolysed by liver enzymes which are a major factor in bioavailability. Orally administered glyceryl trinitrate is ineffective as a therapeutic agent due to first-pass metabolism and administration has therefore routinely been via the sub-lingual route thus bypassing the hepatic circulation initially. 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 administration, initially with ointment preparations but more recently with sustained-release delivery systems provide an alternative route to bypass the hepatic circulation with longer term concentrations of approximately 200pg/ml are achieved within approximately 2h or application of Nitro-Dur and are maintained for 24 h. 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

Adhesive layer covered by PVC Release Liner.

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 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 and other handling

Nitro-Dur patches are applied after removal from the protective pouch. With the brown lines on the backing cover facing the user, edges are bent away to break open the cover along the brown line. The halves of the cover are peeled off and the patch applied firmly to the skin. Hands should be washed thoroughly after application.

Patients should be advised to dispose of patches carefully to avoid accidental application or use.

Administrative Data

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

Nitro-Dur 0.2mg/h : PL 0201/0158

Nitro-Dur 0.4mg/h : PL 0201/0159

Nitro-Dur 0.6mg/h : PL 0201/0160

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22 October 1991 / 09 February 2002

10. DATE OF REVISION OF THE TEXT

January 2005

Legal Category

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