Nytroglycerine-transdermal

Core Safety Profile

4.3 Contraindications

- Known hypersensitivity to nitroglycerin, and related organic nitrates or any excipient of Nitroderm TTS.
- Acute circulatory failure associated with marked hypotension (shock).
- Conditions associated with elevated intracranial pressure.
- Myocardial insufficiency due to obstruction, as in aortic or mitral stenosis or constrictive pericarditis.
- Concomitant use of Nitroderm TTS and phosphodiesterase type 5 (PDE5) inhibitors such as sildenafil (Viagra®) is contraindicated, because PDE5 inhibitors may amplify the vasodilatory effects of Nitroderm TTS resulting in severe hypotension.
- Severe hypotension (systolic blood pressure less than 90 mmHg)
- Severe hypovolemia

4.4 Special warnings and precautions for use

Warnings As with other nitrate preparations, when transferring the patient on long-term therapy to another form of medication, nitroglycerin should be gradually withdrawn and overlapping treatment started.

Nitroderm TTS patch must be removed before applying magnetic or electrical fields to the body during procedures such as MRI (Magnetic Resonance Imaging), cardioversion or DC defibrillation, or diathermy treatment.*

In cases of recent myocardial infarction or acute heart failure, treatment with Nitroderm TTS should be carried out cautiously under strict medical surveillance and/or haemodynamic monitoring.

Removal of the patch should be considered as part of the management of patients who develop significant hypotension.

Precautions Hypoxaemia

Caution should be exercised in patients with arterial hypoxaemia due to severe anaemia (including G6PD deficiency induced forms), because in such patients the biotransformation of nitroglycerin is reduced. Similarly, caution is called for in patients with hypoxaemia and ventilation/perfusion imbalance due to lung disease or ischaemic heart failure. In Patients with alveolar hypoventilation a vasoconstriction occurs within the lung to shift perfusion from areas of hypoxia to of alveolar better ventilated regions the lung (Euler–Liljestrand mechanism). Patients with angina pectoris, myocardial infarction, or cerebral ischaemia frequently suffer from abnormalities of the small airways (especially alveolar hypoxia). Under these circumstances vasoconstriction occurs within the lung to shift perfusion from areas of alveolar hypoxia to better ventilated regions of the lung. As a potent vasodilator, nitroglycerin could reverse this protective vasoconstriction and thus result in increased perfusion of poorly ventilated areas, worsening of the ventilation/perfusion imbalance, and a further decrease in the arterial partial pressure of oxygen.

Hypertrophic cardiomyopathy

Nitrate therapy may aggravate the angina caused by hypertrophic cardiomyopathy.

Increased angina

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

Tolerance to sublingual nitroglycerin

As tolerance to nitroglycerin patches develops, the effect of sublingual nitroglycerin on exercise tolerance may be partially diminished.

***Use of Nitroderm TTS in the prevention of phlebitis**

The infusion site should be examined regularly. If phlebitis develops, it should be treated accordingly.

*** product specific***

4.5 Interaction with other medicinal products and other forms of interaction

Interactions resulting in a concomitant use contraindicated

Concomitant administration of Nitroderm TTS and other vasodilators (e.g PDE5 inhibitors such as sildenafil [Viagra®]) potentiates the blood-pressure-lowering effect of Nitroderm TTS.

Interactions to be considered

Concomitant treatment with calcium antagonists, ACE inhibitors, beta-blockers, diuretics, antihypertensives, tricyclic antidepressants and major tranquillisers may potentiate the blood-pressure-lowering effect of Nitroderm TTS, as may alcohol.

Concurrent administration of Nitroderm TTS with dihydroergotamine may increase the bioavailability of dihydroergotamine. This warrants special attention in patients with coronary artery disease, because dihydroergotamine antagonises the effect of nitroglycerin and may lead to coronary vasoconstriction.

The non-steroidal anti-inflammatory drugs except acetyl salicylic acid may diminish the therapeutic response of Nitroderm TTS.

Concurrent administration of Nitroderm TTS with amifostine and acetyl salicylic acid may potentiate the blood pressure lowering effects of Nitroderm TTS.

4.6 Fertility, pregnancy and lactation

Fertility

There is no data available on the effect of Nitroderm TTS on fertility in humnas.

Pregnancy

Like any drug, Nitroderm TTS should be employed with caution during pregnancy, especially in the first 3 months.

Lactation

There is limited information on the excretion of the active substance in human or animal breast milk. A risk to the suckling child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Nitroderm TTS therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Nitroderm TTS, especially at the start of treatment or dose adjustments, may impair the reactions or might rarely cause orthostatic hypotension and dizziness (as well as exceptionally syncope after overdosing). Patients experiencing these effects should refrain from driving or using machines.

4.8 Undesirable effects

Adverse drug reactions are listed by MedDRA System-Organ Class (SOC). Within each System-Organ Class the adverse drug reactions are ranked by frequency, with the most frequent first. Within each frequency grouping, adverse drug reactions are ranked in order of decreasing seriousness. In addition, the corresponding frequency category, using the following convention (CIOMS III: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1000, < 1/100); rare (≥ 1/10,000, <1/1000); very rare (< 1/10,000), including isolated reports.

Table 1 Adverse drug reactions

Nervous system disorders Common: Headache[1] Very rare: Dizziness

Cardiac disorders

Rare: Tachycardia[2]

Vascular disorders

Rare: Orthostatic hypotension, flushing[2]

Gastrointestinal disorders

Very common: Nausea, vomiting

Skin and subcutaneous tissue disorders

Uncommon: Dermatitis contact

General disorders and administration site conditions

Uncommon: Application site erythema, pruritus, burning, irritation[3]

Investigations

Rare: Heart rate increase

[1] Like other nitrate preparations, Nitroderm TTS commonly causes dose-dependent headaches due to cerebral vasodilatation. These often regress after a few days despite the maintenance of therapy. If headaches persist during intermittent therapy, they should be treated with mild analgesics. Unresponsive headaches are an indication for reducing the dosage of nitroglycerin or discontinuing treatment.

[2] A slight reflex-induced increase in heart rate can be avoided by resorting, if necessary, to combined treatment with a beta-blocker.

[3] Upon removal of the patch, any slight reddening of the skin will usually disappear within a few hours. The application site should be changed regularly to prevent local irritation.

The following adverse drug reactions have been derived from post-marketing experience with Nitroderm TTS via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known. Within each System-Organ Class, adverse drug reactions are presented in order of decreasing seriousness.

- Cardiac disorders: palpitation.
- Skin and subcutaneous tissue disorders: rash generalized.

4.9 Overdose

Signs

High doses of nitroglycerin may lead to severe hypotension and reflex tachycardia or to collapse and syncope. Methaemoglobinaemia has also been reported following accidental overdosage.

Management

The nitrate effect of Nitroderm TTS can be rapidly terminated simply by removing the system(s).

Hypotension or collapse can be treated by elevation or, if necessary, compression bandaging of the patient’s legs.