TROVITE IV INJECTION

DESCRIPTION:
TROVITE IV INJECTION: Ampoule No. 1: Clear, yellow to orange colored solution
TROVITE IV INJECTION: Ampoule No. 2: Clear, colorless to slightly yellow solution

COMPOSITION:
Each 5 ml contains

Ampoule No. 1:		Ampoule No. 2:	
Thiamine HCl BP (Vit B1)	250 mg	Dextrose Monohydrate BP	1000 mg
Pyridoxine HCl BP (Vit B6)	50 mg	Ascorbic Acid BP	500 mg
Riboflavin (Vit B2)	4 mg	Nicotinamide BP	160 mg
		D-Panthenol USP	5 mg

Preservative: Chlorobutanol 25 mg each in Ampoule No. 1 and No. 2

PHARMACODYNAMICS: High potency parenteral vitamins. TROVITE IV INJECTION provides high blood levels of major vitamins intimately involved in co-enzyme systems essential for oxidation reactions in the body as in the Kreb's citric acid cycle. Thiamine deficiencies rapidly lead to a biochemical lesion in the nervous system of experimental animals and in human beings. Single deficiencies of members of the B complex are rare, and TROVITE IV INJECTION supplies all members of the group involved as co-enzymes in carbohydrate metabolism on which the CNS depends for its principal source of energy. Ascorbic acid, the other water soluble vitamin involved in oxidation / reduction reactions, is also included in this formulation.

PHARMACOKINETICS:
Vitamin B1. Thiamine is absorbed from the gastro-intestinal tract and is widely distributed to most body tissues. It is not stored to any appreciable extent in the body and amounts in excess of the body's requirements are excreted in the urine as unchanged thiamine or as metabolites. About 1 mg of thiamine is metabolized in the body daily.

Vitamin B6. Pyridoxine Hydrochloride is rapidly absorbed by the GI tract and rapidly converted in the body into the coenzymes pyridoxal phosphate and pyridoxamine phosphate. These coenzymes play an essential role in protein metabolism. Pyridoxal phosphate forms an essential enzyme for energy production, fat metabolism, central nervous system activity, and haemoglobin production.
Pyridoxal phosphate and L-dopa decarboxylase act as cofactors in the production of dopamine from L-dopa and then noradrenaline via the enzyme dopamine β oxidase. Pyridoxal phosphate also acts as a cofactor in the production of serotonin via 5-hydroxytryptophan. It is believed that sufferers of premenstrual tension have a greatly increased need for pyridoxine due to oestrogen effects on tryptophan metabolism.

Vitamin B2 (Riboflavin). Riboflavin is absorbed from the gastro-intestinal tract, and in the circulation, it is bound to plasma proteins. Although riboflavin is widely distributed little is stored in the body, and amounts in excess of the body's requirements are excreted in the urine. Riboflavin in the faeces is probably the product of intestinal micro-organisms. Riboflavin is converted in the body to flavin mononucleotide (FMN) and then to flavin adenine dinucleotide (FAD).

Nicotinamide. Nicotinamide is readily absorbed from the gastrointestinal tract after oral doses and widely distributed in the body tissues. It appears in breast milk. The main route of metabolism is their conversion to N-methylnicotinamide and the 2-pyridone and 4-pyridone derivatives; nicotinuric acid is also formed. Small amounts of nicotinamide are excreted unchanged in urine after therapeutic doses; however the amount excreted unchanged is increased with larger doses.

D-Panthenol. Dexapanthenol is the corresponding alcohol to Pantothenic acid (Pantonyl-β-alanine, Vitamin B_5). Pantothenic acid is a compound of Co-enzyme A, which is a cofactor for a number of biochemical and enzyme-catalyzed reactions for the transfer of acetyl groups: Composition and decomposition of fatty acids, oxidative metabolism of carbohydrates, biosynthesis and steroids etc.

Co-enzyme A is food compound and is hydrolyzed in the intestines to Pantothenic Acid. Dexapanthenol and D-Panthotenic acid are absorbed rapidly and completely from the small intestines. In the blood, Pantothenic acid is bound to plasma proteins. Inside the cells, Pantothenic acid is transformed to coenzyme A. The substance is eliminated via the kidneys.

Dextrose. Dextrose is absorbed from the gastro-intestinal tract. Three pathways of metabolism are established: glycolysis leading to the formation of pyruvate (aerobic) or lactate (anaerobic), followed by Krebs tricarboxylic acid cycle (citric acid cycle), leading to metabolism to carbon dioxide and water; a pentose phosphate pathway leads also to carbon dioxide and water. Energy is released in these processes. Dextrose is also stored as glycogen in the liver and muscle. Blood-glucose concentrations are maintained, in healthy persons, within normal limits by insulin, which facilitates the passage of glucose through cell membranes, and other homeostatic mechanisms. The body can metabolise about 800 mg per kg body-weight hourly.

Ascorbic. Ascorbic acid is readily absorbed from the gastro-intestinal tract and is widely distributed in the body tissues. The amount present in the body in health is in excess of 1.5 g. The concentration is higher in leucocytes and platelets than in erythrocytes and plasma. In deficiency states the concentration in leucocytes declines later and at a slower rate, and has been considered to be a better criterion for the evaluation of deficiency than the concentration in plasma. Ascorbic acid in excess of the body's needs is rapidly eliminated in the urine and its elimination is usually accompanied by a mild diuresis.

INDICATION: For the rapid treatment of severe vitamin deficiencies which can occur in association with: alcoholism; Wernicke's encephalopathy and Korsa-Koff's psychosis; subacute confusional delirium or amnesic states; specific deficiency syndrome-pellagra, beri-beri, anorexia nervosa; parenteral nutrition, severe malnutrition.

RECOMMENDED DOSAGE:
1) The preferred method of administration of TROVITE IV INJECTION is by drip infusion. Equal volumes of the contents of ampoules number 1 and 2 should be added to 50ml to 100ml physiological saline or glucose 5% and infused over 30 minutes (see storage section).
2) For a combined injection volume of not more than 10ml (e.g. the contents of one 5ml ampoule number 1 and one 5ml ampoule number 2) the contents of the ampoules are drawn up into a syringe to mix them just before use, then injected slowly, over a period of 10 minutes, into a vein.
The dosage used and its duration will depend on the condition.

Adults and elderly:
Rapid therapy of severe depletion or malabsorption of the water soluble vitamins B and C, particularly in alcoholism, where a severe depletion of thiamine can lead to Wernicke's encephalopathy

10 ml solution from Ampoule Number 1	PLUS	10 ml solution from Ampoule Number 2
OR		
15 ml solution from Ampoule Number 1	PLUS	15 ml solution from Ampoule Number 2

2 to 3 pairs of 5 ml ampoules (1 pair = ampoule 1 + ampoule 2) diluted with 50 ml to 100 ml infusion solution (physiological saline or glucose 5%) and administered over 30 minutes every 8 hours, or at the discretion of the physician.

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Psychosis following narcosis or E.C.T; toxicity from acute infections

5 ml Ampoule Number 1	PLUS	5 ml Ampoule Number 2

1 pair of 5 ml ampoules diluted with 50 ml to 100 ml infusion solution (physiological saline or glucose 5%) administered over 30 minutes twice daily for up to 7 days

Haemodialysis

5 ml Ampoule Number 1	PLUS	5 ml Ampoule Number 2

1 pair of 5 ml ampoules diluted with 50 ml to 100 ml infusion solution (physiological saline or glucose 5%) administered over 30 minutes once every two weeks at the end of dialysis.

Children: TROVITE IV INJECTION is rarely indicated for administration to children, however, suitable doses are as follows:
Under 6 years: quarter of the adult dose
6 – 10 years: third of the adult dose
10 – 14 years: half to two thirds of the adult dose
14 years and over: as for the adult dose
Note: Children respond well to vitamins given by mouth in sufficient dosage.

ROUTE OF ADMINISTRATION: Intravenous injection

CONTRAINDICATIONS: Known hypersensitivity to any of the active constituents or to the excipients. TROVITE IV INJECTION should not be administered to patients who are receiving Levodopa for relief of Parkinsonism as the Pyridoxine it contains, nullifies the effect of Levodopa on the central nervous system. Pyridoxine also reduces the plasma levels of anticonvulsants like Phenobarbitone and Phenytoin.

WARNINGS & PRECAUTIONS: Since pyridoxine will antagonize the therapeutic effect of L-dopa, the two preparations should not be administered concurrently. Care to be taken when administering TROVITE IV INJECTION to patients on L-dopa and those with hyperoxaluria since the preparation also contains ascorbic acid.

Although potentially serious allergic adverse reactions such as anaphylactic shock may occur rarely during, or shortly after, parenteral administration of TROVITE IV INJECTION, such rare occurrence of serious allergic reactions should not preclude the use of TROVITE IV INJECTION in patients who need treatment by this route of administration particularly those at risk of Wernicke's encephalopathy – for whom treatment with parenteral thiamine is essential.

Initial warning signs of a reaction to TROVITE IV INJECTION are sneezing or mild asthma and those treating patients need to note that the administration of further injections to such patients may give rise to anaphylactic shock. Facilities for treating anaphylactic reactions should be available whenever TROVITE IV INJECTION is administered. To minimize the risk of such events with TROVITE IV INJECTION, the preferred mode of administration is by infusion over a period of 30 minutes.

This medicine is for injection into a vein only and should not be given by any other route.

Care should be taken to ensure that the route of administration used (intramuscular or intravenous) is that intended – reports of unintentional administration by the wrong route have been received; these incidents have not been associated with serious adverse reactions.

In common with all parenteral products each ampoule should be visually inspected prior to administration and should not be used if particulates are present.

INTERACTION WITH OTHER MEDICAMENTS: The Ascorbic Acid in TROVITE IV INJECTION will interact with Ethinyloestradiol – plasma levels of ethinyloestradiol elevated. Practical significance uncertain. The content of pyridoxine may interfere with the effects of concurrent levodopa therapy.

USE IN PREGNANCY & LACTATION:
Use in pregnancy: No adverse effects have been noted at recommended doses when used as clinically indicated. However animal studies are insufficient with respect to effects on pregnancy / and-or/ embryonal/ foetal development/ and-or/ parturition/ and-or/ postnatal development. The potential risks for human is unknown. Caution should be exercised when prescribing to pregnant women.
Use in lactation: It is not known if this drug is excreted in breast milk, but as many vitamins are, the use of this product in lactating women is not recommended. The potential risk for humans is unknown.

SIDE EFFECTS: Continuous high doses of thiamine may induce paraesthesia and hypotension. Sensitivity to any of the vitamins is rare, however there are cases of hypersensitivity (including anaphylaxis, rash and urticaria) reported. Injection site reactions including pain and swelling.
Post-marketing adverse reactions are reported voluntarily from a population with an unknown rate of exposure. Therefore it is not possible to estimate the true incidence of adverse reactions and the frequency is 'unknown'.

SYMPTOMS AND TREATMENT OF OVERDOSE:
The symptoms of overdosage of Vitamin B1 (Thiamine) are nervousness, convulsion, headaches, weakness, trembling and neuromuscular, paralysis. Withdraw the treatment and give symptomatic and supportive treatment.

INSTRUCTION FOR USE: TROVITE IV INJECTION is suitable for intravenous administration. The contents of each pair of ampoules (i.e. No. 1 and No. 2) should be mixed and used immediately for injection or infusion. The preferred mode of administration is by infusion over a period of 30 minutes.

INCOMPATIBILITIES: This medicinal product must not be mixed with other medicinal products.

STORAGE CONDITIONS:

Injection condition	Storage condition	Other storage instruction
Unopened ampoules	Store below 25ºC. Protect from light. Keep the ampoules in its carton. Do not freeze.	Keep out of reach from children, Jauhkan daripada Kanak-Kanak
Mixed ampoules	Stable up to 4 hours at 25ºC in the light. Discard unused portion	
Dilution with up to 100ml Dextrose 5%	Stable up to 4 hours at 25ºC in the light.	
Dilution with up to 100ml Sodium Chloride 0.9%	Stable up to 4 hours at 25ºC in the light.	

Although no further specific data are available, the solutions are expected to be stable for longer periods when protected from light. Do not freeze.

SHELF LIFE: Please refer to outer package.

PACK SIZE: Pack in a box of 20 ampoules. Consisting 10 ampoules x 5ml Trovite Ampoule 1 and 10 ampoules x 5ml Trovite ampoule 2

PRODUCT REGISTRATION HOLDER & MANUFACTURER:

DUOPHARMA (M) SDN BHD
Lot 2599, Jalan Seruling 59 Kawasan 3,
Taman Klang Jaya, 41200 Klang, Selangor, MALAYSIA.