SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE HUMAN MEDICINAL PRODUCT

DODEX 1000 mcg/ml Solution for IM Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml solution contains
Active substance:
Vitamin B_{12} (cyanocobalamin) 1000 mcg

Excipients:
Benzyl alcohol 15.0 mg
Sodium chloride 9.0 mg
For a full list of excipients, see 6.1.

3. PHARMACEUTICAL FORM

1 ml solution in ampoule
Red, clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
DODEX 1000 mcg/mL IM Ampoule is used for treatment of pernicious anemia, hyperchromic macrocytic anemia due to vitamin B_{12} deficiency, trigeminal neuralgia, sciatic, acute neuritis, neuralgia, shingles and intercostal neuralgias as antineuralgic.
It is also used for diagnostic purposes in Schilling test.

4.2 Posology and method of administration
Posology/frequency and duration of administration:
In acute neuralgia, 500-1000 mcg vitamin B_{12} is administered daily as IM. In acute neuritis and neuralgia, treatment is recommended to be maintained for 10 days. In cases which recur in time, another DODEX cure should be applied.
In pernicious anemia and hyperchromic macrocytic anemia, treatment is initiated with 250-1000 mcg vitamin B_{12} (IM) every other day and this is maintained for 1-2 weeks. Then until it is proved with blood tests that the patient has returned to normal, 250 mcg vitamin B_{12} (IM) is administered once weekly; however, if the patient has neurological complications, 1000 mcg vitamin B_{12} (IM) is continued to be given every other day. When the blood test results of the patient improve, maintenance treatment is implemented by giving 1000 mcg vitamin B_{12} (IM) once monthly.

Method of administration:
DODEX is administered into muscle (IM) via injection according to the frequency, duration and amount of administration indicated above.

Additional information on special populations
Renal/Hepatic insufficiency:
No data available.

Pediatric population:
No data available.

Geriatric population
No data available.

4.3 Contraindications
DODEX is contraindicated
- In patients with hypersensitivity to vitamin B_{12} and its other ingredients,
- In patients with Leber disease.

4.4 Special warning and precautions for use
ONLY FOR INTRAMUSCULAR ADMINISTRATION.

As vitamin B_{12} may mask subacute degeneration of spinal cord, it should not be used without definite diagnosis. Its use in optical neuropathy with high blood vitamin B_{12} concentration is not suitable.

Administration of drugs with suppressing effects on bone marrow (chloramphenicol) upon occurrence of infection, uremia, folic acid or iron deficiency during treatment with vitamin B_{12} may reduce the therapeutic response to cyanocobalamin. Urgent precautions may be required in patients with severe anemia and tissue anoxia. Blood transfusion, high dose of B_{12} and folic acid treatment should be applied to these patients.

In patients with allergic diseases such as asthma, urticaria and eczema, skin test should be made and it should be investigated if the patient has hypersensitivity before administering cyanocobalamin. DODEX should never be administered via intravenous route; it should be administered via intramuscular route.

It should not be used during pregnancy unless vitamin B_{12} deficiency has been demonstrated. Recommended daily vitamin B_{12} dose recommended in pregnancy and breastfeeding is 2.2 and 2.6 mcg. Vitamin B_{12} is excreted in breast milk.

This medicinal product contains 15.0 mg benzyl alcohol in each ampoule. It should not be applied to premature babies and newborns. It may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years of age.

This medicinal product contains less than 1 mmol (23 mg) sodium per ampoule; i.e. is essentially ‘sodium-free’

4.5 Interaction with other medicinal products and other forms of interaction
In patients with vitamin B_{12} deficiency, co-administration of vitamin B_{12} and chloramphenicol may inhibit hematopoietic response to vitamin B_{12}.

Drugs used against infection such as methotrexate, pyrimethamine, colchinine and para-aminosalicylic acid may lead to false results in microbiological blood tests made for the purpose of diagnosis for vitamin B_{12}.

As alcohol reduce the absorption of vitamin B_{12}, consumption of large amounts of alcohol during treatment with vitamin B_{12} may reduce therapeutic response to cyanocobalamine.

Additional information on special populations:
Pediatric population:
No data available.

4.6 Fertility, pregnancy and lactation
General recommendation
Pregnancy category is C.

Women of child-bearing potential/ Contraception
No data available.

Pregnancy
No sufficient data is available regarding the use of DODEX in pregnant women.
Animal studies showed reproductive toxicity (see section 5.3). Potential risk to human is unknown.
DODEX should not be used for the treatment of megaloblastic anemia of pregnancy unless vitamin B_{12} deficiency has been demonstrated.

Breast-feeding
Vitamin B_{12} is secreted into breast milk but this is unlikely to harm the infant. However, patient should ask the doctor for advice.
As benzyl alcohol should not be used in premature babies and new-born infants, mothers who have recently given birth and/or who have premature babies should use DODEX only upon doctor's recommendation.

Reproductive ability/Fertility
No data available.

4.7 Effects on ability to drive and use machines
None.

4.8 Undesirable effects
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (<1/10,000), not known (cannot be estimated based on available data).

Blood and lymphatic system disorders
Not known: Polycytemia vera

Immune system disorders
Not known: Hypersensitivity reactions

Nervous system disorders
Not known: Walking impairment, asthenia, anxiety, dizziness, hypoesthesia, impaired coordination, irritability, paresthesia, headache

Cardiac disorders
Not known: Congestive heart failure, peripheral vascular thrombosis

Respiratory, chest and mediastinal disorders
Not known: Dyspnea, pulmonary edema

Gastrointestinal disorders
Not known: Dyspepsia, nausea, vomiting, mild transient diarrhea, glossitis

Skin and subcutaneous tissue disorders
Rare: Formation or exacerbation of inflammatory acne, formation or exacerbation of folliculitis
Not known: Itching, transient exanthema

Musculoskeletal, connective tissue and bone disorders
Not known: Arthritis, back pain and myalgia

General disorders and administration site conditions
Not known: Swelling in the body, back pain, general pain, pain at the injection site

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9. Overdose
In case of overdose, water soluble vitamins are excreted in urine. There is no specific procedure or antidote for urgent situations.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Vitamin B_{12} (cyanocobalamine and derivatives)
ATC code: B03BA01

Vitamin B_{12} is a vitamin which activates biosyntheses of methionine, thymidine and protoporphyrin and which provides normal erythropoiesis by acting as catalyst in formation of hemoglobin. Due to this effect, it rapidly improves the condition in pernicious anemia and hyperchromic macrocytic anemia.
High dose of Vitamin B_{12} is used in neurological indications such as sciatic and trigeminal neuralgia and rapidly relieves severe pain.

5.2. Pharmacokinetic properties
Absorption
Vitamin B_{12} is absorbed by binding to intrinsic factor. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome, or after gastrectomy.

Distribution
Vitamin B_{12} is extensively bound to plasma proteins. It is stored in the liver. The body retains only 15% of a 1000 mcg dose. 2000-3000 mcg Vitamin B_{12} is readily stored in the body. DODEX enters the enterohepatic circulation via bile secretion.

Metabolism
No data is available regarding the metabolism of parenteral administered Vitamin B_{12}.

Elimination
After injection of cyanocobalamin a large proportion is excreted in the urine within 24 hours.

5.3 Preclinical safety data
The active substance of the drug is being used in clinic practice for many years. Regarding studies are completed. Negative effects which may arise from its use are included in the related sections (4.4, 4.6, 4.8, 4.9).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium chloride
Benzyl alcohol
Water for injection

6.2 Incompatibilities
Information as to drug interactions is indicated in the section numbered 4.5. Cyanocobalamin does not have any incompatibility with the excipients used.

6.3 Shelf life
60 months

6.4 Special precautions for storage
Keep at room temperature below 25°C and protect from light.

6.5 Nature and contents of container
Colorless ampoules of 1 ml, made of Type I glass, printed thereon and with ring.
Each cardboard box contains either 5, 10, 50, 100 or 250 ampoules of 1 ml.

6.6 Special precautions for disposal and other handling
Any unused material should be disposed according to local disposal regulations.

7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No.:1
34303 Küçükçekmece/İSTANBUL - TURKEY

8. MARKETING AUTHORIZATION NUMBER

59/21

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 30.06.1961
Date of last renewal : 15.07.2011

10. DATE OF REVISION OF THE TEXT

21.11.2012