# Vent-Retard® 200

## Anhydrous Theophylline

**COMPOSITION**
Anhydrous theophylline 200 mg; Saccharose 158 mg; Excipient s.q.f. 1 capsule.

**INDICATIONS**
- Bronchial asthma, prevention and treatment.
- Reversible bronchospastic status associated with chronic bronchitis or emphysema.

**DOSAGE**
The dosage schedule will be established by the doctor.
The maximum bronchodilator effect, associated with minimal adverse effects, is achieved with theophylline plasma levels of between 10 and 20 mcg/ml. In some cases a good clinical response can be attained with lower levels (from 5 mcg/ml).
In general, levels higher than 20 mcg/ml are usually associated with a significant incidence of side effects. Owing to wide interindividual variations in theophylline elimination, the adjustment of the dosage must be individualized and established by the doctor.
Due to the special characteristics of the microcapsulated form, which assures a slow general release of theophylline, there will be an interval of 12 hours between administrations, with the dosages being adjusted as indicated below. Higher dosages must only be used with monitoring theophylline plasma levels.
As at the beginning of treatment by oral route transient side effects of a caffeinic type (nausea, restlessness, insomnia, cephalea, diarrhoea or irritability) can be seen, which are unrelated to the plasma level, it is advisable to start the treatment with half of the maximum recommended doses. If the clinical response is insufficient after 3 days and the drug is well tolerated, these doses may be increased at the rate of 25% every 3 days, without exceeding the maximum recommended doses. If the clinical response is inappropriate, the plasma level of theophylline must be determined 3 days after the last increase of the dose, and have the dosage adjusted accordingly.

**Maximum recommended dosages without control of theophylline plasma levels:**

| Adults | Theophylline mg/kg/day |
|---|---|
| Smokers | 15 |
| Non-smokers | 11 |
| Heart failure, cor pulmonale, acute lung oedema | 7 |
| Liver failure | 5 |
| Heart and liver failure | 2 |
| Aged 65 years | 9,5 |

As metabolism of theophylline is quick in children, and is decreasing as they grow until it becomes similar to that of adults towards 16 years of age, the maximum recommended doses are:

| Children | Theophylline mg/kg/day |
|---|---|
| Aged 1-9 years | 21 |
| Aged 9-12 years | 18 |
| Aged 12-16 years | 13 |

**Asthmatic crises:** The use of the intravenous route is recommended in the treatment of severe asthmatic crises. Quick release oral theophyllines may be useful in mild or moderate crises. In these events, if the patient has not received treatment with theophylline in the latest 48 hours, it is advisable to give 5-6 mg/kg as an initial dose. If the patient was already under treatment with theophylline and symptoms of toxicity were not present, then the initial dose will be of 2-3 mg/kg. In both cases the maintenance dosage indicated in the previous section shall be continued.

**GUIDELINES FOR CORRECT ADMINISTRATION**
- The capsules will be taken without being dissolved, chewed or bitten but swallowed with a sufficient quantity of liquid.
- The administration will take place at regular intervals every 12 hours.
- Ingestion of large quantities of drinks with caffeine, such as tea, coffee, cacao and cola, as well as large quantities of chocolate must be avoided. These products may increase the side effects of this drug.

**WARNINGS**
- Occurrence of gastrointestinal or nervous symptomatology does not imply a reliable indication of overdosage. The only sure method of monitoring the dosage is the measurement of theophylline plasma levels.
- Dosages which are not well tolerated by the patient should not be maintained.
- Theophylline does not diffuse into fatty tissue. Adjustment of the dosage in obese patients has to be made according to **their ideal weight.**

- It is important to strictly follow the dosage schedule, specially as far as dosage intervals is concerned.
- If theophylline plasma levels are to be monitored, it must be ensured that the patient has thoroughly fulfilled the dosage schedule in the 3-4 days prior to the analysis.
- It should be taken into account that patients with impaired liver, or congestive heart failure, and those aged over 55 years, eliminate theophylline at a slower speed than normal, therefore lower doses have to be used.
- The habit of smoking increases hepatic theophylline elimination, and smoking patients may require higher doses of the preparation and/or shorter intervals.
- The "retard" or sustained release formulations are all equally effective, but owing to their different pharmacokinetic profiles, they are not interchangeable preparations without previously adjustment of the dosage. Do not change what has been indicated by the doctor without consulting him beforehand.
- This drug contains 158 mg saccharose, therefore precaution should be taken by diabetic patients.

**CONTRAINDICATIONS**
History of hypersensitivity to xanthic bases.

**PRECAUTIONS**
It must be administered with caution in patients with liver impairment, congestive heart failure as well as glaucoma, gastroduodenal ulcer, severe hypertension, hyperthyroidism, severe myocardial lesion, intense hypoxemia, cor pulmonale, or in newborn babies.
Administration during pregnancy should be done only in those cases where the benefit to be obtained justifies the possible risk. Although theophylline may inhibit uterine contractions, it seems not to prolong childbirth in asthmatic women.
Theophylline is being excreted with breast milk, thus lactating mothers have to be warned of the possible symptoms which may appear in the child, such as tachycardia or hyperexcitability.

**INTERACTIONS**
Theophylline may increase excretion of lithium carbonate. Theophylline serum levels are increased by the administration of erythromycin, troleandomycin, lincomycin, clindamycin, cimetidine, allopurinol, oral contraceptives and quinolones (cyprofloxacin, norfloxacin, etc.). Patients taking these substances concurrently with theophylline have to be monitored to prevent a possible overdosage.
Theophylline serum levels are reduced in patients who are being simultaneously administered with aminogluthetimide, phenobarbital, carbamazepine, rifampicin, phenytoin or sulfinpyrazone.
Betablockers and theophylline may have antagonistic pharmacological effects. On the other hand, betablockers reduce the elimination of theophylline.
The concomitant use of ephedrine or other sympathomimetic drugs increases the toxicity of theophylline.
Theophylline may increase the toxicity of digitalis.
Interferences with analytical tests: theophylline may interfere with the determinations of uric acid, of urinary cathecolamines and free fatty acids in plasma. The spectrophotometric methods in determining theophylline serum levels may be altered by: phenylbutazone, furosemide, probenecid, theobromine; tea, coffe or cola beverages, as well as chocolate and paracethamol may induce false high values of theophyllinemia.
The administration of trivalent anti-influenza vaccine may enhance the effect of theophylline.

**SIDE EFFECTS**
These occur most frequently when theophylline plasma levels are higher than 20 mcg/ml.
**Gastrointestinal:** Nausea, vomiting, diarrhoea and epigastric pain.
**Nervous system:** Irritability, restlessness, headache, insomnia, reflex hyperexcitability, muscle contractions. Generalized tonic-clonic convulsions. Behavioural changes.
**Cardiovascular system:** Palpitations, sinusal or ventricular tachycardia, extrasystole or ventricular arrhytmia, peripheral vasodilation and hypotension.
**Other side effects:** Skin rashes, reduction of prothrombin time and increase of serum GOT.
In the event of suspected overdosage, theophylline plasma levels are to be monitored. If this is not possible, the dosage will be reduced or the administration will be discontinued, depending on the severity of the symptoms.

**INTOXICATION AND TREATMENT**
Intoxication may show up through agitation, logorrhea, mental confusion, vomiting, hyperthermia, tachycardia and hypotension. Furthermore, in adults, through convulsions, hyperthermia and cardiac arrest. In the event of accidental massive overdosage, vomiting must be immediately induced. Gastric lavage is indicated if the patient does not have convulsion, as well as the administration of high doses of potential fast-acting laxative drugs and activated carbon.
If the patient has convulsions it is essential to keep the airways unblocked, thus oxygen and diazepam i.v. (0,1 to 0,3 mg/kg up to a total dosage of 10 mg) have to be administered. The vital signs must be monitored. Oxygenation (intubation) must be ensured in comatose conditions after an attack. Hemoperfusion with activated carbon is advisable in case of severe intoxication, in orden to prevent irreversible CNS damage.

**HOW SUPPLIED**
Package containing 40 capsules.

**Under medical prescription.**

**Drugs must be kept out of the reach of children.**

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