SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Vitabiotics Cold and Flu Capsules, hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains
Paracetamol Ph. Eur. 300 mg
Caffeine Ph. Eur. 25 mg
Phenylephrine hydrochloride Ph. Eur. 5 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard (Capsules)

Green and yellow capsule.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of aches, pains, headache, sore throat, fever and nasal congestion associated with colds and influenza.

4.2 Posology and method of administration
Posology

Adults: 1 - 2 capsules every four hours up to a maximum of 4 doses (8 capsules) in any 24 hours. The dosage should not be continued for more than 3 days without consulting a doctor. Dose not to be repeated more frequently than 4 hour intervals.

The Elderly: One capsule every 4 hours.

Children under 12 years of age: Not recommended.

Method of administration
Oral use.

4.3 Contraindications

- Concomitant use of other sympathomimetic decongestants
- Phaeochromocytoma
- Closed angle glaucoma
- Known hypersensitivity to paracetamol or any of the other ingredients.
- Patients with a history of peptic ulcer.
- Hepatic or severe renal impairment
- Hypersusceptible patients or those with hyperthyroidism, aneurism, hypertension, arteriosclerosis, diabetes and cardiovascular disorders.
- As an alpha-adrenoceptor stimulant, it may provoke uterine changes which can result in foetal asphyxia.
- Patients taking tricyclic antidepressants, or beta blocking drugs and those who are taking or who have taken within the last two weeks monoamine oxidase inhibitors (see section 4.5).

4.4 Special warnings and precautions for use

Medical advice should be sought before using this product in patients with these conditions:
- An enlargement of the prostate gland
- Occlusive vascular disease (e.g. Raynaud’s phenomenon)
Cardiovascular disease

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) (see interactions). Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.

Do not exceed the stated dose.

If symptoms persist for more than 3 days consult your doctor.

If you are receiving a course of medicinal treatment, consult your doctor before taking this product.

Contains paracetamol.

Do not give to children under 12 years.

Paracetamol should be given with care to patients with impaired liver or kidney function, and to patients taking other drugs that affects the liver. The hazard of overdose is greater in those with noncirrhotic alcoholic liver disease. Liver function tests may be required at periodic intervals during high dose or long term therapy, especially in patients with pre-existing hepatic disease.

Care should be taken in giving paracetamol to patients with alcohol dependence.

Care should be taken giving paracetamol to patients with glucose-6-phosphate dehydrogenase deficiency.

Caution is advised in patients with cardiovascular disease or those on a sodium restricted diet who should not use buffered paracetamol without medical advice.

Special Label Warnings

Do not take with any other paracetamol-containing products. Do not take with other flu, cold or decongestant products.

Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Special Leaflet Warnings

Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

4.5 Interaction with other medicinal products and other forms of interaction

Enzyme-inducing drugs may increase hepatic damage, as does excessive intake of alcohol. Alcohol and hepatotoxic medications reduce the capacity of the liver to metabolise paracetamol. Cholestyramine reduces absorption of paracetamol. Metoclopramide and domperidone accelerate absorption of paracetamol. Plasma levels of chloramphenicol may increase with concurrent administration of paracetamol. These interactions are considered to be of unlikely clinical significance in acute usage at the dosage regimen proposed. Medical advice should be sought before taking paracetamol-caffeine phenylephrine in combination with the following drugs:

<p>| Non-steroidal anti-inflammatory drugs | Concurrent use of paracetamol with NSAID may increase the risk of adverse renal effects. |</p>
<table>
<thead>
<tr>
<th>(NSAIDs)</th>
<th>Prolonged concurrent use of paracetamol and aspirin or other salicylate may increase the risk of renal damage (such as analgesic nephropathy and renal papillary necrosis).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>Effervescent preparations of paracetamol which contain a high sodium concentration may increase the risk of oedema and/or hypernatraemia when administered concurrently with adrenocorticoids, anabolic steroids, androgens or ACTH.</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Oral tetracyclines may form non-absorbable complexes with the buffering agents present in effervescent preparations; these medications should be taken 1-2 hours apart. The effect of caffeine may be enhanced by isoniazid.</td>
</tr>
<tr>
<td>Tranquilizers (meprobamate)</td>
<td>May enhance the effect of caffeine.</td>
</tr>
<tr>
<td>Monoamine oxidase inhibitors (including moclobemide)</td>
<td>Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine Oxidase inhibitors (see contraindications).</td>
</tr>
<tr>
<td>Sympathomimetic amines</td>
<td>Concomitant use of phenylephrine with other sympathomimetics amines can increase the risk of cardiovascular side effects (see warnings and precautions).</td>
</tr>
<tr>
<td>Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa)</td>
<td>Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased (see contraindications).</td>
</tr>
<tr>
<td>Tricyclic antidepressants (eg amitriptyline)</td>
<td>May increase the risk of cardiovascular side effects with phenylephrine (see contraindications).</td>
</tr>
<tr>
<td>Digoxin and cardiac glycosides</td>
<td>Concomitant use of phenylephrine with digoxin or cardiac glycosides may increase the risk of irregular heartbeat or heart attack.</td>
</tr>
<tr>
<td>Ergot alkaloids (ergotamine and methylsergide)</td>
<td>Increased risk of ergotism. Caffeine is claimed to enhance the action of ergotamines.</td>
</tr>
<tr>
<td>Warfarin and other coumarins</td>
<td>The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with an increased risk of bleeding; occasional doses have no significant effect.</td>
</tr>
</tbody>
</table>
Interactions with laboratory tests: Paracetamol may interfere with a number of test results; blood glucose, urate, bilirubin, lactate dehydrogenase and transaminase concentrations, urine 5-hydroxyindoleacetic acid determination, prothrombin time and pancreatic function using benitromide.

4.6 Fertility, Pregnancy and lactation

This product is not recommended for use in pregnancy due to the phenylephrine and caffeine content.

Paracetamol: Crosses the placenta. There is no known hazard in normal dosage, but like all non-essential medications paracetamol should be avoided especially during the first trimester unless considered essential by the physician. Paracetamol is excreted in breast milk but there is no evidence that this is clinically significant.

Caffeine: During pregnancy, the half-life of caffeine is prolonged. This is a possible contributory factor in hyperemesis gravidarum. It is recommended that no medicines should be taken during pregnancy unless recommended by a doctor. There is a potential increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption during pregnancy. Caffeine in breast milk may have a stimulating effect on breast-fed infants.

Phenylephrine Hydrochloride: Phenylephrine may be excreted in breast milk. As an alpha-adrenoceptor stimulant it may provoke uterine changes which can result in foetal asphyxia.

4.7 Effects on ability to drive and use machines

Phenylephrine hydrochloride may cause drowsiness. Patients should be advised not to drive or operate machinery if affected by dizziness. Avoid alcoholic drinks.

4.8 Undesirable effects

Adverse events of paracetamol from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class. Due to limited clinical trial data, the frequency of these adverse events is not known (cannot be estimated from available data), but post-marketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.
**Paracetamol**

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Undesirable effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Haematological reactions, blood dyscrasias, anaemia, thrombocytopenic purpura, methaemoglobinaemia and agranulocytosis</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Anaphylaxis, cutaneous hypersensitivity reactions including skin rashes, angioedema and Stevens Johnson syndrome, toxic epidermal necrolysis</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Bronchospasm*</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>Hepatic dysfunction, hepatitis, acute pancreatitis</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Renal colic, sterile pyuria, uraemia, azotaemia</td>
</tr>
</tbody>
</table>

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

**Caffeine**

Adverse reactions identified through post-marketing use with caffeine are listed below. The frequency of these reactions is unknown.

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Undesirable effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>Nausea, insomnia, headache, irritability, anxiety, neurosis, restlessness, excitement, muscle tremor, tinnitus, scintillating scotoma, nervousness and dizziness</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Tachycardia, extrasystoles and palpitations</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Increased gastric secretions and may cause gastric ulceration</td>
</tr>
</tbody>
</table>

**Phenylephrine hydrochloride**

The following adverse events have been observed in clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events.

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Undesirable effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric disorders</td>
<td>Nervousness</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache, dizziness, insomnia</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Increased blood pressure</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea, vomiting, diarrhoea</td>
</tr>
</tbody>
</table>

Adverse reactions identified during post-marketing use are listed below. The frequency of these reactions is unknown.
<table>
<thead>
<tr>
<th>System organ class</th>
<th>Undesirable effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye disorders</td>
<td>Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Tachycardia, palpitations</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Perforation of the nasal septum</td>
</tr>
<tr>
<td>Skin and subcutaneous disorders</td>
<td>Allergic reactions (e.g. rash, urticaria, allergic dermatitis) Hypersensitivity reactions – including cross-sensitivity with other sympathomimetics may occur</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy</td>
</tr>
</tbody>
</table>

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation 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 Yellow Card Scheme, Website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)

4.9 **Overdose**

**Paracetamol**

Potentially fatal liver damage is likely in adults who have taken 15 g or more of paracetamol. As little as 10 g may lead to liver necrosis. Patients taking enzyme-inducing drugs or with a history of alcoholism may have an increased susceptibility. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are employed), become irreversibly bound to liver tissue. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

**Risk factors:**

If the patient

a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John’s Wort or other drugs that induce liver enzymes.

Or

b) Regularly consumes ethanol in excess of recommended amounts.

Or

c) Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.
Symptoms:
Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, diarrhoea, anorexia, abdominal pain and increased sweating. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, coma and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management:
Prompt treatment is essential in the management of paracetamol overdosage. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Any patient who has ingested about 7.5 g or more of paracetamol in the preceding 4 hours should undergo gastric lavage or induced emesis. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Specific therapy with an antidote such as acetylcysteine or methionine may be necessary. Acetylcysteine may be given either intravenously or by mouth or methionine may be given by mouth within 10-12 hours of ingestion of the overdose. Generally treatment is required if the blood-paracetamol concentration is higher than a line (the '200' line) drawn on a semi-log/linear paper joining the points 200 mg per litre (1.32 mmol per litre) at 4 hours and 30 mg per litre (0.20 mmol per litre) at 15 hours following ingestion.

Determination of the concentration before 4 hours is not considered to give a reliable measurement. Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. Administration of acetylcysteine or methionine more than 15 hours after the overdose is generally ineffective and may be associated with an exacerbation of any liver abnormality and may precipitate hepatic encephalopathy. Liver function tests should be performed at 24 hour intervals for at least 96 hours post ingestion if the plasma paracetamol concentration indicates a potential for hepatotoxicity. Renal and cardiac function should be monitored and supportive treatment should be directed at maintaining fluid and electrolyte balance and correcting hypoglycaemia. Haemodialysis and haemoperfusion have been used with some success by peritoneal dialysis in ineffective.

Caffeine
Symptoms:
Emesis and convulsions may occur. Overdose of caffeine may result in epigastric pain, vomiting, diurese, tachycardia or cardiac arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related liver toxicity.

Treatment:
No specific antidote is available, but supportive measures may be used. However, treatment is usually fluid therapy. Fatal poisoning is rare. If symptoms become apparent or overdose is suspected, consult a doctor immediately.

**Phenylephrine hydrochloride**

**Symptoms:**
Phenylephrine overdosage is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include hypertension, and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur. However, the amount required to produce serious phenylephrine toxicity would be greater than that required to cause paracetamol-related liver toxicity.

**Treatment:**
Treatment should be as clinically appropriate. Severe hypertension may need to be treated with alpha blocking drugs such as phentolamine. If overdose is suspected, consult a doctor immediately.

5  **PHARMACOLOGICAL PROPERTIES**

5.1  **Pharmacodynamic properties**

*Paracetamol* is an effective analgesic and antipyretic agent but has only weak anti-inflammatory properties. Its mechanism of action is not fully understood. It has been suggested that it may act predominantly by inhibiting prostaglandin synthesis in the CNS and to a lesser extent through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitize pain receptors to mechanical or chemical stimulation. Paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulating centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus. The drug has no effect on the cardiovascular and respiratory systems, and unlike salicylates it does not cause gastric irritation or bleeding.

*Caffeine* acts on the central nervous system on muscle including cardiac muscle and the kidneys. Its action on the CNS is mainly on the higher centres and produces a condition of wakefulness and increased mental activity. It facilitates the performance of muscular work and increases the total amount of work that can be performed by a muscle. It may stimulate the respiratory centre, increasing the rate and depth of respiration. Its stimulant action on the medullary vasomotor centre is usually compensated by its peripheral vasodilator effect on the arterioles, so that blood pressure usually remains unchanged. The diuretic action of caffeine has been accounted for in many ways. It may increase renal blood flow and glomerular filtration rate, but its main action may be due to the regulation of the normal tubular absorption. The xanthines are rarely of great value in promoting increased renal
function when this is depressed. Caffeine is claimed to enhance the action of
ergotamines and is frequently given with ergotamine in the treatment of migraine.

*Phenylephrine hydrochloride* is a sympathomimetic with many direct effects on
adrenergic receptors. It has predominantly alpha-adrenergic activity and is without
stimulating effects on the cns. Its pressor activity is weaker than that of noradrenaline
but of longer duration. After injection it has produced peripheral vasoconstriction and
increased arterial pressure; it also causes reflex bradycardia. It increases blood flow to
the skin and to the kidneys. It has been used in the treatment of hypotensive states eg.
circulatory failure, spinal anaesthesia or hypertension following the use of
chlorpromazine and other phenothiazines. Phenylephrine hydrochloride may be given
for the relief of nasal congestion. Locally it is used as a nasal decongestant in rhinitis
and sinusitis. In ophthalmology it is employed as a mydriatic and conjunctival
decongestant in open angle glaucoma. It is sometimes used to temporarily lower
intra-ocular pressure.

The active ingredients are not known to cause sedation. There is no
pharmacological information with regard to the compound preparation.
However, there is no evidence to suggest that any of the actions described
above are in any way impinged upon by the other active ingredients.

### 5.2 Pharmacokinetic properties

*Paracetamol* is readily absorbed from the gastro-intestinal tract with peak plasma
concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised
in the liver (90-95 %) and excreted in the urine mainly as the glucuronide and
sulphate conjugates. Less than 5 % is excreted as unchanged paracetamol. The
elimination half-life varies from about 1 to 4 hours. Plasma-protein binding is
negligible at usual therapeutic concentrations but increases with increasing
concentrations.

A minor hydroxylated metabolite (n-acetyl-p-benzoquinoneimine) which is usually
produced in very small amounts by mixed-function oxidases in the liver and which is
usually detoxified by conjugation with liver glutathione may accumulate following
paracetamol overdosage and cause liver damage. The time to peak concentrations of
paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of
action 3 to 4 hours.

*Caffeine* is readily absorbed after oral, rectal or parenteral administration, but
absorption from the gastro-intestinal tract may be erratic. The maximal plasma
concentrations are achieved within one hour and the plasma half-life is about 3.5
hours. There is little evidence of accumulation in any particular tissue. Caffeine
passes readily into the central nervous system and into saliva. Concentrations have
also been detected in breast milk. Caffeine is metabolised almost completely. 65-80%
of administered caffeine is excreted in the urine as 1-methyluric acid, 1-
methylxanthine and other metabolises with only about 1 % unchanged.

*Phenylephrine hydrochloride* has reduced bioavailability from the gastro-intestinal
tract owing to first pass metabolism by monoamine oxidase in the gut and liver. It is
excreted in the urine almost entirely as the sulphate conjugate. When injected
intramuscularly it takes 10 to 15 minutes to act and subcutaneous and intramuscular
injections are effective for about an hour. Intravenous injections are effective for
about 20 minutes.
5.3 Preclinical safety data

Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not already been mentioned elsewhere in this Summary.

The toxicity of paracetamol has been extensively studied in numerous animal species. Preclinical studies in rats and mice have indicated single dose oral LD50 values of 3.7 g/kg and 338 mg/kg, respectively. Chronic toxicity in these species at large multiples of the human therapeutic dose, occurs as degeneration and necrosis of hepatic, renal and lymphoid tissue, and blood count changes. The metabolites believed responsible for these effects have also been demonstrated in man. Paracetamol should not, therefore, be taken for long periods of time, and in excessive doses. At normal therapeutic doses, paracetamol is not associated with genotoxic or carcinogenic risk. There is no evidence of embryo-or foetus-toxicity from paracetamol in animal studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch  
Colloidal Anhydrous Silica  
Magnesium Stearate

Capsule Shell contains:  
Gelatin  
Patent Blue V (E131)  
Iron Oxide(E172)  
Quinoline Yellow (E104)  
Titanium Dioxide (E171)

6.2 Incompatibilities

Maize Starch  
Colloidal Anhydrous Silica  
Magnesium Stearate

Capsule Shell contains:
Gelatin
Patent Blue V (E131)
Iron Oxide(E172)
Quinoline Yellow (E104)
Titanium Dioxide (E171)

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.
Keep the blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

PVC blister sealed with aluminium foil.

Pack sizes of 10, 12

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Max Remedies Limited
William Nadin Way
Swadlincote
DE11 0BB
United Kingdom

8  MARKETING AUTHORISATION NUMBER(S)

PL 31308/0039

9  DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25/02/2009

10 DATE OF REVISION OF THE TEXT

01/11/2014