SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Contac Non Drowsy Dual Relief Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Contac Non Drowsy Dual Relief Tablet contains Paracetamol 500 mg and pseudoephedrine hydrochloride 30 mg.

For excipients see Section 6.1

3 PHARMACEUTICAL FORM

Form: Film coated tablet.

Description:

Contac Non Drowsy Dual Relief is a bilayer (white/blue) film coated capsule shaped tablet. The tablet is debossed with the number 2 in a circle on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Contac Non Drowsy Dual Relief is a mild to moderate analgesic, antipyretic and decongestant. Contac Non Drowsy Dual Relief is recommended for the relief from the symptoms of colds and flu including:

- Nasal congestion
- Sore throat pain
- Headache
- Body aches and pains
- Fever
- Sinus symptoms e.g. sinus pain, pressure and congestion

4.2 Posology and method of administration

For oral use.

Adults, including the elderly and children 16 years and over:
Two tablets every four to six hours, to be taken orally. The dose should not be repeated more frequently than every four hours nor should more than three doses be given in any 24-hour period.

Minimum dosing interval: 4 hours Do not exceed the stated dose.

Should not be used with other paracetamol-containing or decongestant products.

Users should be advised to seek medical advice if symptoms persist for more than 7 days.

If pain or fever persist for more than 3 days or get worse, or if any other symptoms occur, treatment should be discontinued, and a physician consulted.

Not to be used in children under 16 years of age.

Elderly patients, especially those who are frail or immobile, may require a reduced dose or frequency of dosing.

Renal impairment:
Patients who have been diagnosed with kidney impairment must seek medical advice before taking this medication. It is recommended, when giving paracetamol to patients with renal failure, to reduce the dose and to increase the minimum interval between each administration to at least 6 hours. The kidney impairment restrictions relate to the use of both paracetamol and pseudoephedrine. (see section 4.4).

Hepatic impairment:
Patients who have been diagnosed with hepatic impairment must seek medical advice before taking this medication. The restrictions related to the use of paracetamol products in patients with hepatic impairment are primarily a consequence of the paracetamol content of the drug (see section 4.4).

4.3 Contraindications

This product is contraindicated in patients.

- With hypersensitivity to paracetamol, pseudoephedrine or excipients
- With severe hypertension or uncontrolled hypertension
- With severe acute or chronic kidney disease/renal failure

- With cardiovascular disease including hypertension or severe coronary artery disease. Who are receiving other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants)

- With hyperthyroidism, prostatic enlargement, diabetes, glaucoma or phaeochromocytoma,

- Who are receiving Monoamine Oxidase Inhibitors (MAOIs), or for two weeks after stopping a MAOI drug

- Who are taking beta-blockers or other anti-hypertensives

4.4 Special warnings and precautions for use

Patients should be advised not to take other paracetamol-containing products concurrently. Immediate medical advice should be sought in the event of overdosage even if the patient feels well because the risk of irreversible liver damage (see section 4.9)

Care is advised in the administration of this product in patients with liver impairment or mild to moderate kidney impairment.

The hazard of overdose is greater in patients with non-cirrhotic alcoholic liver disease.

Caution should also be exercised in patients with arrhythmias.

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)
Cases of PRES and RCVS have been reported with the use of pseudoephedrine-containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure (see section 4.3).
Pseudoephedrine should be discontinued and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances. Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

Paracetamol should be administered only with particular caution to patients at risk of hepatotoxicity at therapeutic doses, i.e. patients who are underweight (adults or adolescents less than 50kg) or of low body mass index, malnourished, dehydrated, those with chronic alcoholism, co-existing renal or hepatic impairment, concomitantly taking hepatotoxic drugs and those with conditions that may predispose to glutathione deficiency or depletion. For some patients considered to be at higher risk, a lower starting dose, a reduction in dose and/or a reduced frequency of dosing may be appropriate (see section 4.2).

Paracetamol should be administered only with particular caution to patients with Glucose-6-phosphate dehydrogenase deficiency who are at risk of haemolysis after exposure to paracetamol.

Ischaemic optic neuropathy
Cases of ischaemic optic neuropathy have been reported with pseudoephedrine. Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.

Risks of abuse
Pseudoephedrine carries the risk of abuse. Increased doses may ultimately produce
toxicity. Continuous use can lead to tolerance resulting in an increased risk of overdosing. The recommended maximum dose and treatment duration should not
be exceeded (see section 4.2).

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism), who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.
Ischaemic colitis
Some cases of ischaemic colitis have been reported with pseudoephedrine.

Pseudoephedrine should be discontinued immediately, and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Keep out of the reach and sight of children.

Precaution should be observed in patients with asthma who are sensitive to acetylsalicylic acid since mild bronchospasms are reported in association with paracetamol (cross reaction).

Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed,

administration of Contac Non-Drowsy Dual Relief should be discontinued and appropriate measures taken if needed.

The stated dose should not be exceeded.

If symptoms persist, medical advice must be sought.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Paracetamol is metabolized in the liver and can therefore interact with other medicines that follow the same pathway or may inhibit or induce this route; causing hepatotoxicity, particularly in overdose (see Section 4.9).

The rate of paracetamol absorption may be reduced by cholestyramine. Cholestyramine should not be administered within one hour of taking paracetamol.

In case of concomitant treatment with probenecid, the dose of paracetamol should be reduced since probenecid reduces the clearance of paracetamol by 50%, as it prevents the conjugation of paracetamol with glucuronic acid.

There is limited evidence suggesting that paracetamol may affect chloramphenicol pharmacokinetics, but its validity has been criticized and evidence of a clinically relevant interaction appears to be lacking. Although no routine monitoring is needed, it is important to bear in mind this potential interaction when these two medications are concomitantly administered, especially in malnourished patients.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis,, especially in patients with risks factors (see section 4.4).

Pseudoephedrine

Concomitant use of this medication with tricyclic antidepressants, sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants), which interfere with the catabolism of sympathomimetic amines, may occasionally cause a rise in blood pressure.

Concomitant use of pseudoephedrine and monoamine oxidase inhibitor (MAOIs) (or within two weeks of stopping of MAOI) may lead to

hypertensive crisis.

Pseudoephedrine may also antagonize the effect of certain classes of antihypertensives (e.g. beta blockers, methyl-dopa, reserpine, debrisoquine, guanethidine). The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Fertility, pregnancy and lactation

Pregnancy

This product should not be used in pregnancy without medical advice.

The safety of paracetamol-pseudoephedrine combination products in pregnancy has not been established despite widespread use over many years.

The product should be avoided during pregnancy, particularly during the first trimester, as defective closure of the abdominal wall (gastroschisis) has been reported very rarely in new-borns after first trimester exposure.

Lactation

Pseudoephedrine is excreted in breast milk, in amounts leading to increased risk of effects in the infants even at therapeutic doses. May suppress lactation. This product should not be used whilst breastfeeding without medical advice.

Pseudoephedrine is excreted in breast milk in small amounts but the effect of thison breast fed infants is unknown.

Fertility

There are no data available regarding the influence of Contac Non-Drowsy Dual Relief Tablets on fertility.

4.7 Effects on ability to drive and use machines

Patients should be advised not to drive or operate machinery if affected by dizziness.

4.8 Undesirable effects

The following convention has been utilized for the classification of undesirable effects; very common (>/=1/10), common (>=1/100, <1/10), common (<=1/1000,
<1/100), rare (>=1/10000, <1/1000), very rare (<1/10000), not known (cannot beestimated from the available data).

Paracetamol

Adverse events 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.

Body System	**Undesirable effect**	**Frequency**
Blood and lymphatic system disorders	Thrombocytopenia, Agranulocytosis	Not known
Immune system disorders	Anaphylaxis	Not known
Metabolism and nutrition disorders	High anion gap metabolic acidosis	Not known
Respiratory, thoracic andmediastinal disorders	Bronchospasm*	Not known
Hepatobiliary disorders	Hepatic dysfunction	Not known
Skin and subcutaneous tissue disorders	Cutaneous hypersensitivity reaction including skin rashes, pruritus, sweating purpura, urticaria and angioedema.	Not known
	Very rare cases of serious skin reaction have been reported.	Very Rare
Renal and disorders	Sterile pyuria (cloudy urine)	Not known

Description of selected adverse reactions

High anion gap metabolic acidosis – Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

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

Pseudoephedrine

The frequency of reactions identified during post-marketing use is not known.

Body System	**Undesirable effect**	**Frequency**
Psychiatric disorders	Nervousness, Insomnia	Not known
	Agitation, Restlessness	Not known
	Hallucinations	Not known
Nervous System Disorders	Dizziness	Not known
	Posterior reversible encephalopathy syndrome (PRES) (see section 4.4) Reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4)	Not known
Eye disorders	Ischaemic optic neuropathy	Not known
Cardiac Disorders	Tachycardia, palpitations	Not known

Vascular Disorders	Increased blood pressure*	Not known
Gastrointestinal Disorders	Vomiting, dry mouth, nausea	Not known
	Ischaemic colitis	Not known
Skin and subcutaneous tissue disorders	Rash, allergic dermatitis**	Not known
	Severe skin reactions, including acute generalized exanthematous pustulosis (AGEP)	Not known
Renal and Urinary Disorders	Dysuria, urinary retention***	Not known

*Increases in systolic blood pressure have been observed. At therapeutic doses, the effects of pseudoephedrine on blood pressure are not clinically significant.
**A variety of allergic skin reactions, with or without systemic features such as bronchospasm and angioedema have been reported following use of pseudoephedrine
***Urinary retention is most likely to occur in those with bladder outlet obstruction,such as prostatic hypertrophy**.**

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

Paracetamol

Liver damage is possible in adults who have taken 10g or more of paracetamol. 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, anorexia and abdominal pain. 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, 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

Immediate treatment is essential in the management of paracetamol overdose. 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.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). 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. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule.

If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

Pseudoephedrine Hydrochloride

Symptoms:

As with other sympathomimetics pseudoephedrine overdose will result in symptoms due to central nervous system and cardiovascular stimulation e.g. excitement, irritability, restlessness, tremor, hallucinations, hypertension, palpitations, arrhythmias and difficulty with micturition. In severe cases, psychosis, convulsions, coma and hypertensive crisis may occur. Serum potassium levels may be low due to extracellular to intracellular shifts in potassium.

Management:

Treatment should consist of standard supportive measures. Beta-blockers should reverse the cardiovascular complications and the hypokalaemia.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code N02B E51

The analgesic and antipyretic actions of paracetamol are believed to be due, at least in part, to inhibition of prostaglandin synthesis in the central nervous system. Paracetamol 1 g has been shown to be an effective analgesic and antipyretic.

Pseudoephedrine is predominantly an indirect-acting sympathomimetic amine. Pseudoephedrine 60 mg has been shown to be an effective nasal decongestant, as measured by nasal airflow, in patients with the common cold and rhinitis.

At therapeutic doses, pseudoephedrine has no clinically significant effect on blood pressure in normotensive patients. Studies in patients with controlled hypertension have demonstrated that pseudoephedrine 60 mg has no, or minimal, effect on blood pressure and does not have sedative effects.

GlaxoSmithKline has conducted a clinical study in patients with symptoms of cold and flu to assess relief of pain and nasal congestion. The study compared Beechams Max Strength Sinus & Pain, **[Paracetamol/Pseudoephedrine Hydrochloride 500mg/30mg Tablets]** (taken three times daily as required for three days) with paracetamol alone, pseudoephedrine alone and placebo. Results demonstrated that Beechams Max Strength Sinus & Pain gives significantly ($p<0.05$) greater pain relief than either placebo or pseudoephedrine and that Beechams Max Strength Sinus & Pain has a significantly ($p<0.05$) greater decongestant effect than either placebo or paracetamol. Beechams Max Strength Sinus & Pain demonstrated an additive effect for relief of pain and nasal congestion compared to paracetamol or pseudoephedrine. For a single dose of Beechams Max Strength Sinus & Pain there was significantly greater ($P<0.05$) relief of pain and nasal congestion (nasal airflow) compared to placebo at one hour post dose.

5.2 Pharmacokinetic properties

Paracetamol

Biotransformation

Paracetamol is rapidly and completely absorbed from the gastro-intestinal tract with peak plasma levels occurring about 0.25-2 hours after dosing. The absolutebioavailability is about 80% and is independent of dose in normal therapeutic doses (5-20 mg/kg). It is not bound to plasma proteins. The volume of distribution is about 0.9 l/kg. The plasma half-life ranges from 1-3 hours and is largely unaffected by age. It is metabolized in the liver and excreted in the urine as the glucuronide and sulphate conjugates.

In overdose situations, saturation of the detoxification of a minor metabolite, N- acetyl-p-benzoquinoneimine, by conjugation with glutathione occurs and this leads to its accumulation and resultant liver damage.

A minor route, catalyzed by the Cytochrome P 450 (mostly CYP2E1), results in the formation of an intermediate reagent (N-acetyl-p-benzoquinoneimine) which under normal conditions of use, is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cysteine and mercapturic acid.

Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

Elimination
Less than 5% is excreted as unmodified paracetamol; the elimination half-life varies from 1 to 4 hours. Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60-80%) and sulphate conjugates (20-30%).

In cases of severe renal impairment (GFR $\leq$ 30 ml/min), the elimination of paracetamol is slightly delayed. For the glucuronide and sulfate conjugates, the elimination rate is 3 times slower in subjects with severe renal impairment than in healthy subjects.

Pseudoephedrine
Pseudoephedrine is rapidly and completely absorbed from the gastrointestinal tract after oral administration, with no presystemic metabolism. Peak plasma levels are achieved after 1-2 hours. No protein binding data are available. The volume of distribution ranges from 2.64 to 3.51 l/kg in both single and multiple dose studies. The plasma half-life varies from 4.3-7.0 hours in adults.

There is little metabolism of pseudoephedrine in man with approximately 90% being excreted in the urine unchanged. Approximately 1% is eliminated by hepatic metabolism, by N-demethylation to norpseudoephedrine.

As a weak base, the extent of renal excretion is dependent on urinary pH. At low urinary pH, tubular resorption is minimal and urine flow rate will not influence clearance of the drug. At high pH (>7.0), pseudoephedrine is extensively reabsorbed in the renal tubule and renal clearance will depend on urine flow rate.

Hepatic disease is unlikely to affect the pharmacokinetics of pseudoephedrine. Renal impairment will result in increased plasma levels. A steady state pharmacokinetic interaction study in healthy volunteers has demonstrated that the rate (Cmax, tmax) and extent (AUC0-6 hours) of absorption from Beechams Max Strength Sinus & Pain tablet **[Paracetamol/Pseudoephedrine Hydrochloride 500mg/30mg Tablet]** is equivalent to those of paracetamol alone and of pseudoephedrine alone.

In the same study the median tmax values for the paracetamol and pseudoephedrine components of Beechams Max Strength Sinus & Pain were 0.7 hours and 1.2 hours, respectively.

5.3 Preclinical safety data

Preclinical safety data on paracetamol and pseudoephedrine in the literature have not revealed findings which are of relevance to the recommended dosage and use of the product and which have not been mentioned elsewhere in the summary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose microcrystalline E 460

Silica, Colloidal anhydrous E 551

Stearic acid E 570

Magnesium stearate E 572

Starch pregelatinised

Povidone

Crospovidone

Croscarmellose sodium E 468

Hydroxypropyl methyl cellulose E 464

Macrogol

Carnauba wax E 903

Indigo carmine E132

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25 deg. C.

6.5 Nature and contents of container

Opaque blister strips of PVC (250 microns)/ PE (25 or 30 microns)/ PVdC 90 g/m2) backed with aluminium foil. Blisters will be packed into cartons and each carton will contain 2, 5, 6, 10, 12, 16, 18, 24, 30 or 32 tablets (not all pack sizes may be marketed).

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Omega Pharma Ltd,
Wrafton, Braunton,
Devon, EX33 2DL,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 02855/0066

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03 December 2002

10 DATE OF REVISION OF THE TEXT

26/03/2025