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APPROVED PACKAGE INSERT

SCHEDULING STATUS:

S2

PROPRIETARY NAME AND DOSAGE FORM:

ADVIL[®] COLD and SINUS (Tablets)

COMPOSITION:

Each tablet contains:

Ibuprofen 200 mg

Pseudoephedrine hydrochloride 30 mg

Contains sugar (sucrose), methyl paraben and propyl paraben in the sugar coating.

The tablets also contain the following excipients: Anhydrous colloidal silica, black printing ink, butterscotch colouring agent (iron oxide red, iron oxide yellow, titanium dioxide), carnauba wax, croscarmellose sodium, maize starch, microcrystalline cellulose, opaglos, povidone, pregelatinised starch, sodium lauryl sulphate, stearic acid and sucrose.

PHARMACOLOGICAL CLASSIFICATION:

A 5.8 Preparation for the common cold including nasal decongestants and antihistaminics.

PHARMACOLOGICAL ACTION:

ADVIL COLD and SINUS has decongestive, analgesic and antipyretic properties.

INDICATIONS:

26 ADVIL COLD and SINUS is indicated for the relief of symptoms associated with the
27 common cold, sinusitis, or flu, including nasal congestion, headache, fever, body aches
28 and pain.

29

30 **CONTRA-INDICATIONS:**

31 ADVIL COLD and SINUS is contra-indicated in:

- 32 • patients sensitive to ibuprofen or any other nonsteroidal anti-inflammatory agent
33 (NSAID)
- 34 • patients sensitive to pseudoephedrine hydrochloride or any other sympathomimetic
35 agent.
- 36 • patients sensitive to any other component of this product
- 37 • persons under treatment with monoamine oxidase inhibitors, or within 14 days of
38 stopping such treatment
- 39 • cardiovascular disease, heart failure, hypertension, diabetes mellitus, hyperthyroidism,
40 hyperexcitability, prostatic hypertrophy, phaeochromocytoma and close-angle
41 glaucoma
- 42 • patients who have had a severe allergic reaction to aspirin - asthma, swelling, shock or
43 hives, because even though ADVIL COLD and SINUS contains no aspirin, or
44 salicylates, cross-reactions may occur in patients allergic to aspirin
- 45 • patients with impaired renal and liver functions
- 46 • patients with a history of gastrointestinal bleeding or perforation related to previous
47 NSAIDs
- 48 • patients with active or history of recurrent ulcer, haemorrhage or perforations
- 49 • patients with bleeding disorders, haematological disorders
- 50 • pregnancy and lactation See "**PREGNANCY AND LACTATION**".

51

52 **WARNINGS and SPECIAL PRECAUTIONS:**

53 Caution is advised to those patients who are receiving coumarin anticoagulants.

54 ADVIL COLD and SINUS should not be combined with other non-prescription pain
55 relievers or any other ibuprofen-containing product.

56 Caution is required in patients with a history of hypertension and/or heart failure as fluid
57 retention and oedema have been reported in association with non-steroidal anti-
58 inflammatory therapy, including ADVIL COLD and SINUS.

59 In view of the inherent potential of ADVIL COLD and SINUS to cause fluid retention, heart
60 failure may be precipitated in some compromised patients.

61 ADVIL COLD and SINUS should be given with caution to patients with a history of
62 gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-
63 oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.

64 The elderly have an increased frequency of adverse reactions to NSAIDs, such as ADVIL
65 COLD and SINUS especially gastrointestinal bleeding and perforation, which may be fatal.

66 The risk of gastrointestinal bleeding or ulceration is higher with increasing doses, in
67 patients with a history of ulcers and the elderly.

68 When gastrointestinal bleeding or ulceration occurs in patients receiving ADVIL COLD and
69 SINUS, treatment should be stopped.

70 Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-
71 Johnson syndrome, and toxic epidermal necrolysis have been reported in association with
72 non-steroidal anti-inflammatory therapy. Discontinue treatment at the first appearance of
73 rash, mucosal lesions, or any other sign of hypersensitivity.

74

75 **Special Precautions:**

76 **Ibuprofen:**

77 Ibuprofen should be discontinued in patients who experience blurred or diminished vision
78 or changes in colour vision.

79 Aseptic meningitis has occurred in patients with systemic lupus erythematosus who were
80 receiving ibuprofen.

81 **Pseudoephedrine hydrochloride:**

82 To minimise the possibility of insomnia, the last dose for each day should be administered
83 a few hours before bedtime.

84

85 **INTERACTIONS:**

86 **Ibuprofen:**

87 Interactions involving NSAIDs include possible enhancement of the effects of oral
88 anticoagulants (such as warfarin) and increased plasma concentrations of lithium,
89 methotrexate and digoxin.

90 The risk of nephrotoxicity may be increased if ADVIL COLD and SINUS is given with
91 angiotensin-converting enzyme inhibitors, cyclosporine, tacrolimus or diuretics.

92 There may also be an increased risk of hyperkalaemia with angiotensin-converting enzyme
93 inhibitors and potassium-sparing diuretics.

94 The antihypertensive effects of some antihypertensive agents including angiotensin-
95 converting enzyme inhibitors, beta blockers, and diuretics may be reduced.

96 Convulsions may occur due to an interaction with quinolones.

97 ADVIL COLD and SINUS may enhance the effects of phenytoin, oral antidiabetic agents
98 and insulin.

99 The risk of gastrointestinal bleeding and ulceration associated with ADVIL COLD and
100 SINUS is increased when used with corticosteroids, selective serotonin reuptake inhibitors,
101 the antiplatelets clopidogrel and ticlopidine, or, possibly alcohol, bisphosphonates, or
102 oxpentifylline (pentoxifylline).

103 The concomitant use of more than one NSAID (including aspirin) should be avoided
104 because of the increased risk of adverse effects.

105 There may be an increased risk of haemotoxicity during concomitant use of zidovudine and
106 ADVIL COLD and SINUS.

107 **Pseudoephedrine hydrochloride:**

108 Pseudoephedrine hydrochloride should be given with caution to patients receiving
109 halothane or other halogenated anaesthetics.

110 An increased risk of dysrhythmias may occur if pseudoephedrine hydrochloride is given to
111 patients receiving digoxin, quinidine or tricyclic antidepressants and there is an increased
112 risk of vasoconstrictor or pressor effects in patients receiving ergot alkaloids or oxytocin.

113 Pseudoephedrine hydrochloride may reverse the action of many antihypertensive agents
114 and therefore special care is advisable in patients receiving antihypertensive therapy.

115 Pseudoephedrine may cause a hypertensive crisis in patients receiving a monoamine
116 oxidase inhibitor (MAOI). See "**CONTRA-INDICATIONS**".

117 Concurrent use with beta-adrenergic blocking agents may inhibit the therapeutic effect of
118 these agents, with a risk of hypertension and excessive bradycardia and possible heart
119 block.

120 Concurrent use with citrates may inhibit urinary excretion and prolong the duration of action
121 of pseudoephedrine.

122 Concurrent use with central nervous system (CNS) stimulation-producing medications may
123 result in additive CNS stimulation to excessive levels.

124 The use of levodopa with pseudoephedrine may increase the possibility of cardiac
125 dysrhythmias.

126 Concurrent use of nitrates with pseudoephedrine may reduce the anti-anginal effects of
127 these medications.

128 The use of thyroid hormones and pseudoephedrine concurrently may increase the effects
129 of either these medications or pseudoephedrine.

130 In addition to possibly increasing CNS stimulation, concurrent use with other
131 sympathomimetics may increase the cardiovascular effects and the potential for side-
132 effects.

133

134 **PREGNANCY AND LACTATION:**

135 ADVIL COLD and SINUS is not recommended for use in pregnant or lactating women.

136 **Ibuprofen:**

137 Regular use of non-steroidal anti-inflammatory drugs during the third trimester of
138 pregnancy, may result in premature closure of the foetal ductus arteriosus in utero, and
139 possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may
140 be delayed and its duration increased.

141 **Pseudoephedrine hydrochloride:**

142 Pseudoephedrine studies on birth defects have not been done in humans.

143 However, studies in animals have shown pseudoephedrine causes a reduction in average
144 weight, length and rate of bone formation in the animal foetus.

145 Pseudoephedrine passes into breast milk and may cause unwanted effects in nursing
146 babies.

147

148 **DOSAGE AND DIRECTIONS FOR USE:**

149 **Adults and Children 12 years and older:**

150 Take one tablet every 4 to 6 hours. If symptoms do not respond to one tablet, a second
151 tablet may be taken. Do not exceed 6 tablets in 24 hours.

152 ADVIL COLD and SINUS should be taken with a glass of water, with food or after meals.

153 Not to be given to children under 12 years.

154 Do not take for cold for more than 7 days or for fever for more than 3 days, unless directed
155 by a doctor. If the cold or fever persists or gets worse, or if new symptoms occur, consult a
156 doctor.

157 Use the lowest effective dose for the shortest possible duration of treatment.

158

159 **SIDE EFFECTS:**

160 **Ibuprofen:**

161 **Blood and the lymphatic system disorders:**

162 *Less frequent:* Agranulocytosis, anaemia, aplastic anaemia, eosinophilia, leukopenia,
163 neutropenia, thrombocytopenia, haemolytic anaemia.

164 *Frequency unknown:* Ecchymosis.

165 **Immune system disorders:**

166 *Less frequent:* Anaphylaxis or anaphylactoid reactions, angitis, angioedema;
167 bronchospastic allergic reactions, allergic rhinitis, serum sickness-like reaction, systemic
168 lupus erythematosus-like syndrome, hepatotoxicity and aseptic meningitis, which may
169 occur rarely, may also be hypersensitivity reactions.

170 **Nervous System Disorders:**

171 *Frequent:* Dizziness

172 *Less frequent:* Mild to moderate headache, nervousness or irritability,
173 confusion, hallucinations, aseptic meningitis, mental depression, peripheral neuropathy,
174 drowsiness, trouble in sleeping.

175 *Frequency unknown:* Convulsions, mood or mental changes.

176 **Eye disorders:**

177 *Less frequent:* Amblyopia (toxic), blurred or double vision or change in vision, conjunctivitis;
178 dry, irritated or swollen eyes.

179 **Ear and labyrinth disorders:**

180 *Less frequent:* Ringing or buzzing in ears; decrease or change in hearing.

181 **Cardiac disorders:**

182 Many of the cardiovascular effects may occur secondary to NSAID-induced renal function
183 impairment.

184 *Less frequent:* Oedema, hypertension, unexplained nose bleeds; cardiac dysrhythmias;
185 congestive heart failure or exacerbation of; fast or pounding heartbeat; flushing.

186 *Frequency unknown:* Angina pectoris or exacerbation of; pulmonary oedema.

187 **Gastrointestinal disorders:**

188 *Frequent:* Mild to moderate abdominal cramps; pain or discomfort; epigastric pain or
189 discomfort; heartburn, nausea.

190 *Less frequent:* Flatulence, constipation, decreased appetite or loss of appetite; diarrhoea,
191 indigestion, vomiting, gastritis, gastrointestinal bleeding or haemorrhage; melaena,
192 haematemesis, gastrointestinal perforation, gastrointestinal ulceration, irritation, dryness or
193 soreness of mouth. Gingival ulceration or aphthous stomatitis.

194 *Frequency unknown:* Colitis or exacerbation of; enterocolitis, oesophagitis, ulcerative
195 stomatitis, exacerbation of Crohn's disease.

196 **Hepato-biliary disorders:**

197 *Less frequent:* Pancreatitis, hepatitis or jaundice (toxic).

198 *Frequency unknown:* Abnormalities in liver function tests.

199 **Skin and subcutaneous tissue disorders:**

200 *Frequent:* Skin rash.

201 *Less frequent:* Itching, bullous eruption, hives, Stevens-Johnson syndrome, toxic epidermal
202 necrolysis, erythema multiforme.

203 *Frequency unknown:* Eczema, exfoliative dermatitis, photosensitivity reactions.

204 **Respiratory, thoracic and mediastinal disorders:**

205 See also "Immune system disorders"

206 *Less frequent:* Alveolitis, pulmonary eosinophilia, pulmonary oedema.

207 **Renal and urinary disorders:**

208 *Less frequent:* Fluid retention; oedema. unexplained vaginal bleeding, blood in urine;
209 cystitis; renal impairment or failure; polyuria, renal papillary or tubular necrosis.

210 *Frequency unknown:* Renal calculi or ureteral obstruction; interstitial nephritis, nephrotic
211 syndrome.

212

213 **Pseudoephedrine hydrochloride:**

214 **Endocrine disorders:**

215 *Frequency unknown:* Altered metabolism, including disturbances of glucose metabolism.

216 **Nervous System disorders:**

217 *Frequent:* Nervousness, restlessness, insomnia.

218 *Less frequent:* Giddiness, headache, sweating, muscular weakness, tremor, hallucinations,
219 convulsions.

220 *Frequency unknown:* Fear, confusion, irritability, psychotic states, tolerance with
221 dependence may occur.

222 **Cardiac disorders:**

223 *Less frequent:* Tachycardia.

224 *Frequency unknown:* Precordial pain, palpitations, hypertension and ventricular
225 dysrhythmias may occur.

226 **Respiratory, thoracic and mediastinal disorders:**

227 *Less frequent:* Shortness of breath or troubled breathing.

228 *Frequency unknown:* Dyspnoea.

229 **Gastrointestinal disorders:**

230 *Less frequent:* Nausea or vomiting.

231 *Frequency unknown:* Reduced appetite, thirst, ischaemic colitis.

232 **Skin and subcutaneous tissue disorders:**

233 *Frequency unknown:* Skin rashes

234 **Renal and urinary disorders:**

235 *Less frequent:* Difficult or painful urination.

236 *Frequency unknown:* Urinary retention.

237

238 **KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:**

239 See "**SIDE EFFECTS**".

240 Treatment is symptomatic and supportive.

241 The latest information regarding the treatment of overdose can be obtained from the
242 nearest poison control centre.

243

244 **IDENTIFICATION:**

245 A butterscotch coloured, oval-shaped, sugar-coated tablet with a polished surface and
246 "ADVIL COLD & SINUS" printed on one side.

247

248 **PRESENTATION:**

249 Cartons containing aluminium foil/clear PVC film blister packs of 10 or 20 tablets.

250

251 **STORAGE INSTRUCTIONS:**

252 Store at or below 25 °C. Protect from light and exposure to air.

253 KEEP OUT OF REACH OF CHILDREN.

254

255 **REGISTRATION NUMBER:**

256 Z/5.8/248

257

258 **NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF**

259 **REGISTRATION:**

260 Pfizer Laboratories PFE (Pty) Ltd

261 85 Bute Lane

262 Sandton, 2196

263 South Africa

264

265 **DATE OF PUBLICATION OF THIS PACKAGE INSERT:**

266 20 April 2012

267

Botswana Reg. No. : 0400687
Schedule : 3
Namibia Reg. No. : 04/5.8/1008
Schedule : NS0

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