ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORM, STRENGTHS OF THE MEDICINAL PRODUCTS, ROUTE OF ADMINISTRATION, MARKETING AUTHORISATION HOLDERS IN THE MEMBER STATES

Member State	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Austria	Novartis Consumer Health-Gebro GmbH, Bahnhofbichl 13 6391 Fieberbrunn/Tirol, Austria Attn: Dr. D. Werner Attn: Dr. Volker Eisenreich	Mega-Calcium-Brausetabletten	Ca 1000mg	Effervescent tablets	Oral use
Austria	Novartis Consumer Health-Gebro GmbH, Bahnhofbichl 13 6391 Fieberbrunn/Tirol, Austria Attn: Dr. D. Werner Attn: Dr. Volker Eisenreich	Calcium "Sandoz" forte - Brausetabletten	Ca 500mg	Effervescent tablets	Oral use
Belgium	Novartis Consumer Health SA/NV Medialaan, 30 Bus 5 - 1800 VILVOORDE Belgium Attn: Mr Pieter De Pourcq	SANDOZ CALCIUM, comprimés effervescents	Ca 500mg	Effervescent tablets	Oral use
Cyprus	Varnavas Hadjipanayis Ltd. 7A Androcleous Str. 1060 Nicosia Cyprus. Attn: G. Tseriotis	Calcium-Sandoz® forte 500mg	Ca 500mg	Effervescent tablets	Oral use
Czech Republic	Novartis s.r.o. Divison Consumer Health Nagano III. U Nákladového nádraží 10	CALCIUM-SANDOZ® FF 1000mg	Ca 1000mg	Effervescent tablets	Oral use

	130 00 Praha3 Czech Republic Attn: Ugo Di Francesco & Dr. H. Blehova				
Czech Republic	Novartis s.r.o. Divison Consumer Health Nagano III. U Nákladového nádraží 10 130 00 Praha3 Czech Republic Attn: Ugo Di Francesco & Dr. H. Blehova	CALCIUM-SANDOZ® FORTE 500mg	Ca 500mg	Effervescent tablets	Oral use
Denmark	Novartis Healthcare A/S, Lyngbyvej 172, 2100 Kobenhavn, Denmark Attn: J. Grevsen	Calcium-Sandoz, brusetabletter	Ca 500mg	Effervescent tablets	Oral use
Finland	Novartis Finland Oy, Metsänneidonkuja 10, 02130 Espoo, Finland Attn: Mr Torbjörn Sonck & Ms Eeva Liisa Kärkkäinen	Mega-Calcium 1g Ca^{2+} poretabletti	Ca 1000mg	Effervescent tablets	Oral use
Finland	Novartis Finland Oy, Metsänneidonkuja 10, 02130 Espoo, Finland Attn: Mr Torbjörn Sonck & Ms Eeva Liisa Kärkkäinen	Calcium-Sandoz 500mg Ca^{2+} poretabletti	Ca 500mg	Effervescent tablets	Oral use
France	Novartis Santé Familiale S.A.S., 14 Bld Richelieu 92845 Rueil Malmaison Cedex,	CALCIUM SANDOZ 500mg, comprimés effervescents	Ca 500mg	Effervescent tablets	Oral use

	France Attn: M. Lours				
Germany	Novartis Consumer Health GmbH, Zielstattstrasse 40, 81379 München, Germany Attn: Dr. M. Unkauf	Calcium-Sandoz® fortissimum 1000mg	Ca 1000mg	Effervescent tablets	Oral use
Germany	Novartis Consumer Health GmbH, Zielstattstrasse 40, 81379 München, Germany Attn: Dr. M. Unkauf	Calcium-Sandoz® forte 500mg	Ca 500mg	Effervescent tablets	Oral use
Greece	Novartis (Hellas) AEBE 12o Km National Road No1, 14451 Metamorfosis Attikis, Greece Attn: C. Hatzidakis	Mega-Calcium® Sandoz	Ca 1000mg	Effervescent tablets	Oral use
Hungary	Novartis Hungária Kft. Consumer Health 1027 Budapest Horvát u. 14-24. II. Emelet Postacím: 1525 Budapest, Pf. 118 Hungary Attn: P. Miko	Calcium-Sandoz pezsgõtabletta	Ca 500mg	Effervescent tablets	Oral use
Iceland	Novartis Healthcare A/S, Lyngbyvej 172, 2100 Kobenhavn, Denmark Attn: J. Grevsen	Calcium-Sandoz, freyðitöflur	Ca 500mg	Effervescent tablets	Oral use
Ireland	Novartis Consumer Health UK Ltd, Wimblehurst Road, Horsham, West Sussex RH12 5AB	Sandocal 1000	Ca 1000mg	Effervescent tablets	Oral use

	United Kingdom Attn: Dr Jacinta Keogh-Bennett				
Italy	Novartis Consumer Health S.p.A, Largo U. Boccioni, 1 21040 Origgio (VA), Italy Attn: Ms Maria Carla Baggio & Mr Carlo Candiani	CALCIUM-SANDOZ 1000mg compresse effervescenti	Ca 1000mg	Effervescent tablets	Oral use
Italy	Novartis Consumer Health S.p.A, Largo U. Boccioni, 1 21040 Origgio (VA), Italy Attn: Ms Maria Carla Baggio & Mr Carlo Candiani	CALCIUM-SANDOZ 500mg compresse effervescenti	Ca 500mg	Effervescent tablets	Oral use
Luxembourg	Novartis Consumer Health SA/NV Medialaan, 30 Bus 5 - 1800 VILVOORDE Belgium Attn: Mr Pieter De Pourcq	Calcium-Sandoz® fortissimum 1000mg	Ca 1000mg	Effervescent tablets	Oral use
The Netherlands	Novartis Consumer Health B.V, Claudius Prinsenlaan 140 4818 CP Breda, Netherlands Attn: W. VanBerckel	Sandoz Calcium fortissimum, bruistabletten	Ca 1000mg	Effervescent tablets	Oral use
The Netherlands	Novartis Consumer Health B.V, Claudius Prinsenlaan 140 4818 CP Breda, Netherlands Attn: W. VanBerckel	Sandoz Calcium forte, bruistabletten	Ca 500mg	Effervescent tablets	Oral use
Norway	Novartis Norge A/S Consumer Health, Brynsalléen 4	Calcium-Sandoz® 500mg effervescent	Ca 500mg	Effervescent tablets	Oral use

	Postboks 237 Økern 0510 Oslo, Norway Attn: J. Lam				
Poland	Novartis Consumer Health GmbH, Zielstattstrasse 40, 81379 München, Germany Attn: Mr Martin Bischof & Dr. Markus Unkauf	CALCIUM-SANDOZ Forte	Ca 500mg	Effervescent tablets	Oral use
Portugal	NCH Produtos Farmaceuticos e Nutriçao Lda, Av. Poeta Mistral n°2-2°, 1069-172 Lisboa, Portugal Attn: Ms Maria do Céu Correia & Ms Margarida Moraes	CALCIUM-SANDOZ® FORTE 500mg	Ca 500mg	Effervescent tablets	Oral use
Slovakia	Novartis s.r.o. Divison Consumer Health Nagano III. U Nákladového nádraží 10 130 00 Praha3 Czech Republic Attn: Ugo Di Francesco & Dr. H. Blehova	CALCIUM-SANDOZ® Forte	Ca 500mg	Effervescent tablets	Oral use
Slovakia	Novartis s.r.o. Divison Consumer Health Nagano III. U Nákladového nádraží 10 130 00 Praha3 Czech Republic Attn: Ugo Di Francesco & Dr. H. Blehova	CALCIUM-SANDOZ® FF 1000mg	Ca 1000mg	Effervescent tablets	Oral use

Slovenia	Medis, d.o.o. P.O. 2646, Brnčičeva 1 1000 Ljubljana, Slovenia Mr Tone Strnad	Calcium-Sandoz Forte	Ca 500mg	Effervescent tablets	Oral use
Spain	Novartis Consumer Health SA, Gran Via Corts Catalanes 764, 08013 Barcelona Spain Attn: A. Catasus	Calcium Sandoz Forte comprimidos efervescentes	Ca 500mg	Effervescent tablets	Oral use
Sweden	Novartis Sverige AB Consumer Health, Kemistvägen 1B, PO Box 1150 183 11 Täby, Sweden Attn: R. Sigerud	Calcium-Sandoz 1 g brustablett	Ca 1000mg	Effervescent tablets	Oral use
Sweden	Novartis Sverige AB Consumer Health, Kemistvägen 1B, PO Box 1150 183 11 Täby, Sweden Attn: R. Sigerud	Calcium-Sandoz 500mg brustablett	Ca 500mg	Effervescent tablets	Oral use
United Kingdom	Novartis Consumer Health UK Ltd, Wimblehurst Road, Horsham, West Sussex RH12 5AB United Kingdom Attn: Dr Jacinta Keogh-Bennett	SANDOCAL 1000	Ca 1000mg	Effervescent tablets	Oral use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF CALCIUM SANDOZ EFFERVESCENT TABLETS (AND ASSOCIATED NAMES – SEE ANNEEX 1)

Novartis Consumer Health SA acting on behalf of all Marketing Authorisation holders (see Annex I) has applied for harmonisation according to Article 30 of 2001/83/EC, as amended, of their products Calcium Sandoz 500 mg effervescent tablets (Calcium lactate gluconate + Calcium carbonate 1132 + 875 mg) and Calcium Sandoz 1000 mg effervescent tablets
(Calcium lactate gluconate + Calcium carbonate 2263 + 1750 mg). The scope of the procedure were the necessary measures to achieve an harmonised Summary of Product Characteristics (SPC), and the harmonisation of module 3 of the dossier, for which the Marketing Authorisation Holder proposed to replace all existing formulas with a single formula in two strengths, and to optimize the manufacturing process for this formula.

The following quality, efficacy and safety issues were addressed:

- Quality issues

The quality of this product is considered to be acceptable when used in accordance with the conditions defined in the SPC. Physicochemical and biological aspects relevant to the uniform clinical performance of the product have been investigated and are controlled in a satisfactory way.

- Efficacy issues

Calcium is an essential mineral, necessary for bone formation and maintenance, for electrolyte equilibrium in the body and for the proper functioning of numerous regulatory mechanisms.
It was agreed that the wording indication would address the following three conditions: a generally worded indication for *prevention and treatment of calcium deficiency*, which covers situations of expected/potential increased calcium demand. *Osteoporosis*, where the role of calcium supplementation is well established. Successful treatment of *rickets and osteomalacia* will require adequate supply and action of vitamin D and sufficient supply of calcium to allow normal bone mineralisation.

- Safety issues

Based on the available information and a literature search, there does not seem to be any major safety issue associated with the administration of calcium in oral use. However, several amendments to the SPC were introduced.
Section on contraindications remained unchanged. Calcium Sandoz is therefore contraindicated in patients with hypersensitivity to the active substances or to any of the excipients of the effervescent tablet; diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria; nephrocalcinosis and nephrolithiasis.
Minor wording modification was introduced to section on pregnancy and lactation in order to add clarity and to put it in line with the guideline on summary of product characteristics.
Section on undesirable effects was amended according to last post marketing surveillance information, and brought also in line with the guideline on summary of product characteristics. Classification and terminology were amended according to the MedDRA system organ class.

Benefit/Risk considerations

The active ingredients of the medicinal products, Calcium Sandoz 500 mg and 1000 mg effervescent tablets (calcium lactate gluconate and calcium carbonate), have demonstrated efficacy and an acceptable level of safety during decades of human use in a large number and variety of products in numerous countries.

Based on the documentation submitted by the Marketing Authorisation Holders and the scientific discussion within the Committee, the CHMP considered that the benefit/risk ratio of Calcium Sandoz 500 mg and 1000 mg effervescent tablets is positive for the agreed and harmonised indications.

GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS

Whereas,

- the scope of the referral was the harmonisation of the Summary of Product Characteristics, and harmonisation of the pharmaceutical documentation – module 3 (quality)
- the Summary of Products Characteristic proposed by the Marketing Authorisation Holders has been assessed based on the documentation submitted and the scientific discussion within the Committee,

the CHMP has recommended the amendment of the Marketing Authorisations for which the Summary of Product Characteristics is set out in Annex III of this opinion.

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Calcium Sandoz and associated names (see Annex 1) 500 mg, effervescent tablets
Calcium Sandoz and associated names (see Annex 1) 1000 mg, effervescent tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet of 500 mg contains:
1132 mg of calcium lactate gluconate and 875 mg of calcium carbonate (equivalent to 500 mg or 12.5 mmol of calcium).
Each effervescent tablet of 1000 mg contains:
2263 mg of calcium lactate gluconate and 1750 mg of calcium carbonate (equivalent to 1000 mg or 25 mmol of calcium).
For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent tablet
White, circular, flat faced, bevelled edge effervescent tablets with an orange odour

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Prevention and treatment of calcium deficiency
- Calcium supplement as an adjunct to specific therapy in the prevention and treatment of osteoporosis
- Rickets and osteomalacia, in addition to vitamin D_3 therapy

4.2 Posology and method of administration

Adults: 500 – 1500 mg per day
Children: 500 – 1000 mg per day
The effervescent tablets should be dissolved in a glass of water (approx. 200 ml) and drunk immediately. Calcium Sandoz effervescent tablet may be taken with or without food.

4.3. Contraindications

- Hypersensitivity to the active substances or to any of the excipients of the effervescent tablet
- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria
- Nephrocalcinosis, nephrolithiasis

4.4. Special warnings and precautions for use

For patients with mild hypercalciuria (exceeding 300 mg/24 hours or 7.5 mmol/24 hours), or with a history of urinary calculi, monitoring of calcium excretion in the urine is required. If necessary, the calcium dose should be reduced or therapy should be discontinued. An increased fluid intake is recommended for patients prone to formation of calculi in the urinary tract.
In patients with impaired renal function, calcium salts should be taken under medical supervision with monitoring of calcium and phosphate serum levels.
During high dose therapy and especially during concomitant treatment with vitamin D, there is a risk of hypercalcaemia with subsequent kidney function impairment. In these patients serum calcium levels should be followed and renal function should be monitored.

There have been literature reports alluding to possible increased absorption of aluminium with citrate salts. Calcium Sandoz effervescent tablet (which contains citric acid) should be used with caution in patients with severely impaired renal function, especially those also receiving aluminium-containing preparations.
Each Calcium Sandoz effervescent tablet contains aspartame, a source of phenylalanine equivalent to 15 mg/dose**,** and may be harmful for people with phenylketonuria.
Patients with rare hereditary problems of fructose intolerance or glucose-galactose malabsorption should not take this medicine.
Calcium Sandoz 500 mg contains 2.976 mmol (corresponding to 68.45 mg) of sodium per tablet.
Calcium Sandoz 1000 mg contains 5.95 mmol (corresponding to 136.90 mg) of sodium per tablet.
Calcium Sandoz effervescent tablets should be kept out of the reach of children.
Information for diabetics:
One effervescent tablet contains 0.002 Carbohydrate Units and is therefore suitable for diabetics.

4.5. Interaction with other medicinal products and other forms of interaction

Thiazide diuretics reduce the urinary excretion of calcium. Due to increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.
Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of Calcium Sandoz.
Tetracycline preparations administered concomitantly with calcium preparations may not be well-absorbed. For this reason, tetracycline preparations should be administered at least two hours before or four to six hours after oral intake of calcium.
Cardiac glycoside toxicity may increase with hypercalcaemia resulting from treatment with calcium. Patients should be monitored with regard to electrocardiogram (ECG) and serum calcium levels.
If an oral bisphosphonate or sodium fluoride is used concomitantly, this preparation should be administered at least three hours before the intake of Calcium Sandoz since gastrointestinal absorption of either oral bisphosphonate or sodium fluoride may be reduced.
Oxalic acid (found in spinach and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption through formation of insoluble compounds with calcium ions. The patient should not take calcium products within two hours of eating foods high in oxalic acid and phytic acid.

4.6. Pregnancy and lactation

The adequate daily intake (including food and supplementation) for normal pregnant and lactating women is 1000-1300 mg calcium.
During pregnancy, the daily intake of calcium should not exceed 1500 mg. Significant amounts of calcium are secreted in milk during lactation but do not cause any adverse effects to the neonate.
Calcium Sandoz effervescent tablets can be used during pregnancy and lactation in case of a calcium deficiency

4.7. Effects on ability to drive and use machines

Calcium Sandoz has no influence on the ability to drive and use machines.

4.8. Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: *uncommon* (>1/1,000, <1/100), *rare* (>1/10,000, <1/1,000) or *very rare* (<1/10,000), including isolated reports.
Immune system disorders:
Rare: Hypersensitivity, such as rash, pruritus, urticaria.
Very rare: Isolated cases of systemic allergic reactions (anaphylactic reaction, face oedema, angioneurotic oedema) have been reported
Metabolism and nutrition disorders:
Uncommon: Hypercalcaemia, hypercalciuria

Gastrointestinal disorders:
Rare: flatulence, constipation, diarrhoea, nausea, vomiting, abdominal pain

4.9. Overdose

Overdose leads to hypercalciuria and hypercalcaemia. Symptoms of hypercalcaemia may include: nausea, vomiting, thirst, polydipsia, polyuria, dehydration and constipation. Chronic overdose with resulting hypercalcaemia can cause vascular and organ calcification.
The threshold for calcium intoxication is from supplementation in excess of 2000 mg per day, taken for several months.
Treatment of overdose:
In the case of an intoxication, treatment should be stopped immediately and the fluid deficiency should be corrected.
In case of chronic overdose where hypercalcaemia is present, the initial therapeutic step is hydration with saline solution. A loop diuretic (e.g., furosemide) may then be used to further increase calcium excretion and to prevent volume overload, but thiazide diuretics should be avoided. In patients with renal failure, hydration is ineffective and they should undergo dialysis. In the case of persistent hypercalcaemia, contributing factors should be excluded, e.g., vitamin A or D hypervitaminosis, primary hyperparathyroidism, malignancies, renal failure, or immobilisation.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Mineral supplements
ATC codes: Calcium carbonate (A 12 AA 04), Calcium lactate gluconate (A 12 AA 06)
Calcium is an essential mineral, necessary for bone formation and maintenance, for electrolyte equilibrium in the body and for the proper functioning of numerous regulatory mechanisms.

5.2 Pharmacokinetic properties

Calcium Sandoz contains two calcium salts, calcium lactate gluconate and calcium carbonate, which readily dissolve in water to make the active ionised form of calcium freely usable.
Absorption:
Some 25-50% of the ingested dose of calcium is absorbed, predominantly in the proximal part of the small intestine, and delivered to the exchangeable calcium pool.
Distribution and metabolism:
The mineral component of bones and teeth contains 99% of the body's calcium. The remaining 1% is present in the intra- and extracellular fluids. About 50% of the total blood-calcium content is in the physiologically active ionised form, with approximately 5% being complexed to citrate, phosphate or other anions. The remaining 45% of serum calcium is bound to proteins, principally albumin.
Elimination:
Calcium is excreted in the urine, faeces and sweat. Urinary excretion depends on glomerular filtration and tubular reabsorption.

5.3 Preclinical safety data

There is no information of relevance to the safety assessment in addition to what is stated in other parts of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Citric acid anhydrous (fine granulate)
Orange flavour powder (contains: orange essential oils, maltodextrin, arabic gum, sorbitol (E 420), dextrose)
Aspartame (E951)
Macrogol 6000
Sodium hydrogen carbonate

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2 years.

6.4. Special precautions for storage

Keep the tube tightly closed. Store in the original package.

6.5. Nature and contents of container

The effervescent tablets are packed in polypropylene tubes and tamperproof polyethylene stoppers with desiccant, each containing 10 or 20 tablets. The tubes are packed in boxes containing 10, 20, 30, 40, 60, 80, 100 and 600 (for 500 mg only) tablets.
Not all pack sizes may be marketed.

6.6 instructions for use and handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

To be completed nationally.

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

To be completed nationally.

10. DATE OF REVISION OF THE TEXT