

RESTRICTED

MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey

Number : E-62820468-000-480055 Subject : Medicines Containing Acetyl Salicylic Acid Alone or in Combination NORMAL

07.07.2021 DOSSIER Ref: Our association decision dated 12.02.2021, with No. E.-24931227-000-314415.

The sections reading “2-Products containing only Acetyl Salicylic Acid (75 mg, 80 mg, 81 mg, 100 mg, 150 mg, 300 mg)” and “3-For 500 mg Acetyl Salicylic Acid” in our association announcement regarding products containing Acetyl Salicylic Acid Alone or in Combination have been arranged and the referred association decision is updated as indicated below: • Association announcement dated 19.07.2007 on “Preparations Containing Combination of Acetyl Salicylic Acid and Ascorbic Acid”, • Association announcement dated 20.04.2009, on “Acetyl Salicylic Acid Preparations”, • Association announcement dated 06.02.2012, with No. 0012552 and job tacking No. 549646, on “Preparations Containing Acetyl Salicylic Acid”, • Association announcement dated 07.08.2014, with No. 95839 and job tacking No. 1391881, on “Preparations Containing Acetyl Salicylic Acid”, • Association announcement dated 30.09.2014, with No. 117489 and job tacking No. 1445084 on “Preparations Containing Acetyl Salicylic Acid”. • Association announcement dated 12.01.2021, with No. E-24931227-000-314415, on “Medicines Containing Acetyl Salicylic Acid Alone or in Combination” have been re- evaluated by the Clinical Evaluation Commission on Medicinal Products for Human Use” and it has been decided to revoke the referred association decisions. • Furthermore, it is suitable for all preparations containing acetylsalicylic acid alone or in combination to be prescription-only. 1-General Provisions: a- The upper limits on what may be contained in the indications specific to the active substance content of each medicinal product have been designated below. Registration applicants may declare one, some, or all of these indications relating to the product referred to in the circular in the indications section of the product; however, they should not add a new indication other than these. b- In case of statements mentioning the “age limit for children/adults” in the indications of the products, it is mandatory for registration applicants to remove the statements on age from this section, add the following note instead of these, and indicate in the relevant section what is required by this note. “See section 4.4. Special warnings and precautions of the product on children and adolescents.”

Note: Registration applicants may declare the upper age limit where desired provided that they do not go below the age limit indicated for children in their declarations on critical age groups. 2- The indications should be as follows for products containing only Acetylic salicylic acid (75 mg, 80 mg, 81 mg, 100 mg, 150 mg, 300 mg):

SUMMARY OF PRODUCT CHARACTERISTICS It may be used, - As part of standard treatment in unstable angina pectoris, - As part of standard treatment in acute myocardial infarction, - In reinfarction prophylaxis, - Following the operations and other interventions related to arterial blood vessels [Percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG)], - In the prevention of transient ischemic attacks and cerebral infarction in risky patient groups, - In Kawasaki disease; o For reducing inflammation in the febrile period, o As a prophylactic in the prevention of thrombocyte aggregation in coronary aneurysm.

PACKAGE LEAFLET - As part of standard treatment in chest pain occurring at rest/not associated with movement (unstable angina pectoris), - As part of standard treatment in sudden heart attack (acute myocardial infarction), - In the protection against recurrence of heart attack (reinfarction), - In the prevention of vascular occlusion and clots following cardiovascular surgeries, - In the prevention of temporary paralysis and strokes in risky patient groups, - In vasculitis frequently developing in young children under the age of five and characterized with fever, skin rash, strawberry tongue, red and cracked lips, redness in the palms of the hands and the soles of the feet (Kawasaki disease), o For reducing inflammation in the febrile period o In the prevention

of blood clotting in of abnormal expansion (aneurism) in the walls of blood vessels feeding the heart. 2- The posology for products containing only Acetyl Salicylic acid (75 mg, 80 mg, 81 mg, 100 mg, 150 mg, 300 mg) should be as follows: - Once-daily 75-300 mg as part of standard treatment in unstable angina pectoris, - Once-daily 75-300 mg as part of standard treatment in acute myocardial infarction, - Once-daily 75-300 mg in reinfarction prophylaxis,

- Once-daily 75-300 mg following the operations and other interventions related with arterial blood vessels [Percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG)], - Once-daily 75-300 mg in the prevention of transient ischemic attacks and cerebral infarction in risky patient groups, - In Kawasaki disease. o Treatment should be continued at 30-50 mg/kg or at a dose of 80-100 mg/kg for reducing inflammation in the febrile period at a frequency of 3-4 doses per day until the fever drops or for 14 days. The maximum dose should be 4 g/day. o It should be used prophylactically at a dose of 3-5 mg/day in the prevention of thrombocyte aggregation in coronary aneurysms.

3- a) The indications should be as follows for 500 mg Acetylsalicylic acid: “- In mild-moderate pain, - Fever, - See section 4.4. Special warnings and precautions of the product on children and adolescents.” 3- b) The indications should be as follows for 500 mg Acetylsalicylic acid:

SUMMARY OF PRODUCT CHARACTERISTICS Posology: “It should be used at a maximum dose of 4 mg as 1-2 tablets (equivalent to 500-1,000 mg acetylsalicylic acid) at an interval of 4-8 hours in adolescents aged 16 years and above and adults.” Frequency and duration of use: “It should not be used for longer than 4 days without consulting a physician. In case of See section ‘4.4 Special warnings and precautions for use’ in case of inadvertent use of the medication.”

PACKAGE LEAFLET Instructions for adequate use and frequency of dose/administration: “Unless otherwise suggested by your doctor, it should be used at a maximum daily dose of 8 tablets (4 mg) at once as 1-2 tablets at an interval of 4-8 hours for adolescents aged 16 years and above. Do not take for longer than 4 days or at a high dose without consulting your doctor.”

4-The indications for Acetylsalicylic acid + Ascorbic acid (Vitamin C) or citric acid should be as follows (The upper limits for the active substance amount should be 500 mg for ASA + 250 mg for Vitamin C, respectively): “It is indicated in pain and fever associated with cold and flu in adolescents aged 16 and above and adults.” 5- The indications for Acetylsalicylic acid + Pseudoephedrine should be as follows (The upper limits for the active substance amount should be 500 mg for ASA + 30 mg for Pseudoephedrine, respectively).

All precautions relating to pseudoephedrine should be arranged in line with the Association announcement dated 15.03.2018, with No. E.50239 on “Medicines containing pseudoephedrine salts”: “It is indicated in case of nasal congestion where fever is accompanied by pain and cold and flu accompanied by mild body pain in adolescents aged 16 years and above and adults”.

SUMMARY OF PRODUCT CHARACTERISTICS The following statement should be included in 4.4. Special warnings and precautions for use: “It should be used with caution in patients aged above 60 years, with hypertension, hyperthyroidism, diabetes mellitus, cardiovascular disease, ischemic heart disease, glaucoma, kidney failure, or prostate hypertrophy (hyperplasia). It should not be used for longer than five days.”

PACKAGE LEAFLET The statement mentioned in the section “USE ... CAREFULLY in the following conditions” should be arranged as follows: “It should be used with caution in patients aged above 60 years, with hypertension, hyperthyroidism, diabetes, cardiovascular disease, ischemic heart disease (disease which develops due to malnutrition of heart muscle), glaucoma (elevation in intraocular pressure), kidney failure, or prostate enlargement. It should not be used for longer than five days.” 6-The indications for Acetylsalicylic acid + Caffeine should be as follows: (The upper limits for the active substance amount should be 500 mg ASA + 65 mg Caffeine, respectively) “It is indicated for mild to moderate acute pain and febrile conditions in adolescents aged 16 years and above and adults.” 7- The indications for Acetylsalicylic acid + Paracetamol + Caffeine should be as follows: [The total upper limit of both active substances in the combination of ASA + Paracetamol should not surpass 500 mg (their individual amount should not be less than

200 mg) + the upper limit of Caffeine should be 65 mg. In combination preparations containing paracetamol, the daily dose of paracetamol should not surpass 2 grams in those taking alcohol and 4 grams in those not taking alcohol.]

SUMMARY OF PRODUCT CHARACTERISTICS “It is indicated in mild to moderate pains such as headache, dental pain, acute migraine attacks, neuralgia, musculoskeletal system pains, and dysmenorrhea, and conditions accompanied by pain such as cold in adolescents aged 16 years and above and adults. See section 4.4. Special warnings and precautions for use” of the product for children and adolescents.”

PACKAGE LEAFLET “It is indicated in mild to moderate pains such as headache, dental pain, acute migraine attacks, neuralgia, musculoskeletal system pains and dysmenorrhea and conditions accompanied by pain such as cold in adolescents aged 16 years and above and adults. See section 4.4. Special warnings and precautions for use” of the product for children and adolescents.” 8- Only one of the following statements specific to the product should be written in addition to “It should not be used without the physician’s recommendation in children” in the part on children in section 4.4. Special warnings and precautions for use in the SPC of the products:

- In combination products containing ASA: “Its use is not recommended under the age of 16 years unless there is a specific indication.” - In products containing only ASA: “Its use is not recommended under the age of 16 years unless there is a specific indication (such as Kawasaki disease).” 9-All statements related to indications, posology, warnings-precautions within the scope of this announcement shall be adequately reflected in the Package Leaflet as well. I hereby submit for your information and kindly request for the conduct of relevant action so that any view, proposal, and contribution on the decision adopted is submitted to the Clinical Evaluation Unit within 10 (ten) days as of the publication date of this association announcement decision and that no application is submitted to the Pharmacological Evaluation Unit and Registration Unit regarding the “Medicines Containing Acetyl Salicylic Acid Alone or in Combination” during the referred process. Spec. Pharm. Oğuzhan KOYUNCU on behalf of the President of the Agency Head of Department

Distribution: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association Association of Innovator Pharmaceutical Companies Self-Care Products Association Turkish Foundation on Pharmaceuticals, Pharmacy, Health Sciences and Technologies

MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey REVOKED

NORMAL

12.01.2021

Number : 62820468-000-E.24931227-000- Subject : Medicines Containing Acetyl Salicylic Acid Alone or in Combination

DOSSIER

Ref: Our decision for Associations, dated 16.01.2020, with No. E. 12525.

The section on “2-Products containing only Acetyl Salicylic Acid (75 mg, 80 mg, 81 mg, 100 mg, 150 mg, 300 mg)” in our association announcement regarding products containing acetylsalicylic acid alone or in combination has been amended in line with the decision adopted by the “Clinical Evaluation Commission of Medicinal Products for Human Use” of our Agency, and the updated association decision is presented below. It has been decided to revoke the following association decisions upon their re-evaluation by the “Clinical Evaluation Commission of Medicinal Products for Human Use”: • Association announcement dated 19.07.2007 on “Preparations Containing Combination of Acetyl Salicylic Acid and Ascorbic Acid”, • Association announcement dated 20.04.2009, on “Acetyl Salicylic Acid Preparations”, • Association announcement dated 06.02.2012, with No. 0012552 and job tacking No. 549646, on “Preparations Containing Acetyl Salicylic Acid”, • Association announcement dated 07.08.2014, with No. 95839 and job tacking No.

1391881, on "Preparations Containing Acetyl Salicylic Acid", • Association announcement dated 30.09.2014, with No. 117489 and job tacking No. 1445084 on "Preparations Containing Acetyl Salicylic Acid". • Association announcement dated 04.04.2019, with No. E. 56366 on "Medicines containing acetylsalicylic acid alone or in combination", • Association announcement dated 16.01.2020, with No. E.12525, on "Medicines containing acetylsalicylic acid alone or in combination". • Furthermore, it is suitable for all preparations containing acetylsalicylic acid alone or in combination to be prescription-only medicines. 1-General Provisions: c- The upper limits on what may be contained in the indications specific to the active substance content of each medicinal product have been designated below. Registration applicants may declare one, some, or all of these indications relating to the product referred to in the circular in the indications section of the product; however, they should not add a new indication other than these.

d- In case of statements indicating the "age limit for children/adults" in the indications of the products, it is mandatory for registration applicants to remove the statements on age from this section, add the following note instead of these, and indicate in the relevant section what is required by this note. "See section 4.4. Special warnings and precautions for use of the product for children and adolescents." Note: Registration applicants may declare the upper age limit where desired provided that they do not go below the age limit indicated for children in their declarations on critical age groups. 2- The indications should be as follows for products containing only Acetylic salicylic acid (75 mg, 80 mg, 81 mg, 100 mg, 150 mg, 300 mg):

SUMMARY OF PRODUCT CHARACTERISTICS It may be used, - As part of standard treatment in unstable angina pectoris, - As part of standard treatment in acute myocardial infarction, - In reinfarction prophylaxis, - Following the operations and other interventions related to arterial blood vessels [Percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG)], - In the prevention of transient ischemic attacks and cerebral infarction in risky patient groups, - In Kawasaki disease; o For reducing inflammation in the febrile period, o As a prophylactic in the prevention of thrombocyte aggregation in coronary aneurysm.

PACKAGE LEAFLET - As part of standard treatment in chest pain occurring at rest/not associated with movement (unstable angina pectoris), - As part of standard treatment in sudden heart attack (acute myocardial infarction), - In the protection against recurrence of heart attack (reinfarction), - In the prevention of vascular occlusion and clots following cardiovascular surgeries, - In the prevention of temporary paralysis and strokes in risky patient groups, - In vasculitis frequently developing in young children under the age of five years and characterized by fever, skin rash, strawberry tongue, red and cracked lips, redness in the palms of the hands and the soles of the feet (Kawasaki disease), o For reducing inflammation in the febrile period o In the prevention of blood clotting in of abnormal expansion (aneurism) in the walls of blood vessels feeding the heart.

3- The indications should be as follows for 500 mg. Acetylsalicylic acid:

"- In mild-moderate pains, - Fever, See section 4.4. Special warnings and precautions for use for children and adolescents." 4-The indications for Acetylsalicylic acid + Ascorbic acid (Vitamin C) or citric acid should be as follows (The upper limits for the active substance amount should be 500 mg ASA + 250 mg Vitamin C, respectively): "It is indicated in pain and fever associated with cold and flu in adolescents aged 16 years and above and adults." 5- The indications for Acetylsalicylic acid + Pseudoephedrine should be as follows (The upper limits for the active substance amount should be 500 mg ASA + 30 mg Pseudoephedrine, respectively. All precautions relating to pseudoephedrine should be arranged in line with the Association announcement dated 15.03.2018, with No. E.50239 on "Medicines containing pseudoephedrine salts": "It is indicated in case of nasal congestion where fever is accompanied by pain and cold and flu accompanied by mild body pain in adolescents aged 16 years and above and adults".

SUMMARY OF PRODUCT CHARACTERISTICS The following statement should be included in section 4.4. Special warnings and precautions for use: "It should be used with caution in patients aged above 60 years, with hypertension, hyperthyroidism, diabetes mellitus, cardiovascular

disease, ischemic heart disease, glaucoma, kidney failure, or prostate hypertrophy (hyperplasia). It should not be used for longer than five days.”

PACKAGE LEAFLET The statement mentioned in the section “USE ... CAREFULLY in the following conditions” should be arranged as follows: “It should be used with caution in patients aged above 60 years, with hypertension, hyperthyroidism, diabetes, cardiovascular disease, ischemic heart disease (disease which develops due to malnutrition of heart muscle), glaucoma (elevation in intraocular pressure), kidney failure, or prostate enlargement. It should not be used for longer than five days.” 6-The indications for Acetylsalicylic acid + Caffeine should be as follows: (The upper limits for the active substance amount should be 500 mg ASA + 65 mg Caffeine, respectively) “It is indicated for mild to moderate acute pain and febrile conditions in adolescents aged 16 years and above and adults.” 7- The indications for Acetylsalicylic acid + Paracetamol + Caffeine should be as follows: [The total upper limit of both active substances in the combination of ASA + Paracetamol should not surpass 500 mg (their individual amount should not be less than 200 mg) + the upper limit of Caffeine should be 65 mg. In combination preparations containing paracetamol, the daily dose of paracetamol should not surpass 2 grams in those taking alcohol and 4 grams in those not taking alcohol.]

SUMMARY OF PRODUCT CHARACTERISTICS “It is indicated in mild to moderate pains such as headache, dental pain, acute migraine attacks, neuralgia, musculoskeletal system pains and dysmenorrhea and conditions accompanied by pain such as cold in adolescents aged 16 and above and adults. See section 4.4. Special warnings and precautions for use” of the product for children and adolescents.”

PACKAGE LEAFLET “It is indicated in mild to moderate pains such as headache, dental pain, acute migraine attacks, neuralgia, musculoskeletal system pains and dysmenorrhea and conditions accompanied by pain such as cold in adolescents aged 16 years and above and adults. See section 4.4. Special warnings and precautions for use of the product for children and adolescents.” 8- Only one of the following statements specific to the product should be written in addition to “It should not be used without the doctor’s recommendation in children” in the part on children in section 4.4. Special warnings and precautions for use in the SPC of the products: - In combination products containing ASA: “Its use is not recommended under the age of 16 years unless there is a specific indication.” - In products containing only ASA: “Its use is not recommended under the age of 16 years unless there is a specific indication (such as Kawasaki disease).” 9-All statements related to indications, posology, warnings-precautions within the scope of this announcement should be adequately reflected in the Package Leaflet as well. The SPC/PL applications related to the products in which the abovementioned amendments are made should be submitted to the Pharmacological Evaluation Unit within 1 month as of the publication date of this announcement decision for review, the applications related to the products with ongoing registration process should be submitted to the Registration Unit and this announcement should be taken into account for products for which a registration application will be made. I hereby submit for your information and kindly request for the conduct of relevant action so that the referred applications are not submitted to the Clinical Evaluation Unit. Assoc. Prof. Dr. Tolga TOLUNAY President of the Agency

Distribution: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association Association of Innovator Pharmaceutical Companies Self-Care Products Association

REVOKED RESTRICTED

MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey

Number : 62820468-000-E.12525 Subject : Medicines containing acetylsalicylic acid alone or in combination NORMAL

16.01.2020 DOSSIER

Ref: Our decision for Associations, dated 04.04.2019, with No. E. 56366.

The section on “2-Products containing only Acetyl Salicylic Acid (75 mg, 80 mg, 81 mg, 100 mg, 150 mg, 300 mg)” in our association announcement regarding products containing acetylsalicylic acid alone or in combination” has been amended in line with the decision adopted by the “Clinical Evaluation Commission of Medicinal Products for Human Use” of our Agency and the updated association decision is provided below. It has been decided to revoke the following association decisions upon their re-evaluation by the “Clinical Evaluation Commission of Medicinal Products for Human Use”: • Association announcement dated 19.07.2007 on “Preparations Containing Combination of Acetyl Salicylic Acid and Ascorbic Acid”, • Association announcement dated 20.04.2009, on “Acetyl Salicylic Acid Preparations”, • Association announcement dated 06.02.2012, with No. 0012552 and job tacking No. 549646, on “Preparations Containing Acetyl Salicylic Acid”, • Association announcement dated 07.08.2014, with No. 95839 and job tacking No. 1391881, on “Preparations Containing Acetyl Salicylic Acid”, • Association announcement dated 30.09.2014, with No. 117489 and job tacking No. 1445084 on “Preparations Containing Acetyl Salicylic Acid”. • Furthermore, it is suitable for all preparations containing acetylsalicylic acid alone or in combination to be prescription-only medicines. 1-General Provisions: a- The upper limits on what may be contained in the indications specific to the active substance content of each medicinal product have been designated below. Registration applicants may declare one, some, or all of these indications relating to the product referred to in the circular in the indications section of the product; however, they should not add a new indication other than these. b- In case of statements indicating the “age limit for children/adults” in the indications of the products, it is mandatory for registration applicants to remove the statements on age from this section, add the following note instead of these, and indicate in the relevant section what is required by this note. Note: Registration applicants may declare the upper age limit where desired provided that they do not go below the age limit indicated for children in their declarations on critical age groups.

2- The indications should be as follows for products containing only Acetylic salicylic acid (75 mg, 80 mg, 81 mg, 100 mg, 150 mg, 300 mg):

SUMMARY OF PRODUCT CHARACTERISTICS It may be used, - As part of standard treatment in unstable angina pectoris, - As part of standard treatment in acute myocardial infarction, - In reinfarction prophylaxis, - Following the operations and other interventions related to arterial blood vessels [Percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG)], - In the prevention of transient ischemic attacks and cerebral infarction in risky patient groups, - In Kawasaki disease; o For reducing inflammation in the febrile period, o As a prophylactic in the prevention of thrombocyte aggregation in coronary aneurysm. - For the purpose of preventing cardiovascular events to all persons who fulfill the following conditions in people with no atherosclerotic cardiovascular disease: o Patients aged between 40-70 years, o With a 10-year cardiovascular event risk of more than 10% (SCORE risk calculation, etc.), o With a low bleeding potential.

PACKAGE LEAFLET - As part of standard treatment in chest pain occurring at rest/not associated with movement (Unstable angina pectoris), - As part of standard treatment in sudden heart attack (Acute myocardial infarction), - In the protection against recurrence of heart attack (reinfarction), - In the prevention of vascular occlusion and clots following cardiovascular surgeries, - In the prevention of temporary paralysis and strokes in risky patient groups, - In vasculitis frequently developing in young children under the age of five and characterized with fever, skin rash, strawberry tongue, red and cracked lips, redness in the palms of the hands and the soles of the feet (Kawasaki disease), o For reducing inflammation in the febrile period o In the prevention of blood clotting in of abnormal expansion (aneurism) in the walls of blood vessels feeding the heart. - It may be used for the purpose of preventing cardiovascular events to all persons who fulfill all of the following conditions in people with no atherosclerotic cardiovascular disease: o Patients aged between 40-70 years, o With a 10-year cardiovascular event risk of more than 10% (SCORE risk calculation, etc.),

o With a low bleeding potential.

3- The indications should be as follows for 500 mg. Acetylsalicylic acid: “- In mild-moderate pain, - Fever, - See section 4.4. Special warnings and precautions for use for children and adolescents.” 4-The indications for Acetylsalicylic acid + Ascorbic acid (Vitamin C) or citric acid should be as follows: (The upper limits for the active substance amount should be 500 mg ASA + 250 mg Vitamin C, respectively.) “It is indicated in pain and fever associated with cold and flu in adolescents aged 16 years and above and adults.” 5- The indications for Acetylsalicylic acid + Pseudoephedrine should be as follows (The upper limits for the active substance amount should be 500 mg for ASA + 30 mg for Pseudoephedrine, respectively. All precautions relating to pseudoephedrine should be arranged in line with the Association announcement dated 15.03.2018, with No. E.50239 on “Medicines containing pseudoephedrine salts”: “It is indicated in case of nasal congestion where fever is accompanied by pain and cold and flu accompanied by mild body pain in adolescents aged 16 and above and adults”).

SUMMARY OF PRODUCT CHARACTERISTICS The following statement should be included in section 4.4. Special warnings and precautions for use: “It should be used with caution in patients aged above 60 years, with hypertension, hyperthyroidism, diabetes mellitus, cardiovascular disease, ischemic heart disease, glaucoma, kidney failure, or prostate hypertrophy (hyperplasia). It should not be used for longer than five days.”

PACKAGE LEAFLET The statement mentioned in the section “USE ... CAREFULLY in the following conditions” should be arranged as follows: “It should be used with caution in patients aged above 60 years, with hypertension, hyperthyroidism, diabetes, cardiovascular disease, ischemic heart disease (disease which develops due to malnutrition of heart muscle), glaucoma (elevation in intraocular pressure), kidney failure, or prostate enlargement. It should not be used for longer than five days.” 6-The indications for Acetylsalicylic acid + Caffeine should be as follows: (The upper limits for the active substance amount should be 500 mg for ASA + 65 mg for Caffeine, respectively) “It is indicated for mild to moderate acute pain and febrile conditions in adolescents aged 16 years and above and adults.” 7- The indications for Acetylsalicylic acid + Paracetamol + Caffeine should be as follows: [The total upper limit of both active substances in the combination of ASA + Paracetamol should not surpass 500 mg (their individual amount should not be less than 200 mg) + the upper limit of Caffeine should be 65 mg. In combination preparations containing paracetamol, the daily dose of paracetamol should not surpass 2 grams in those taking alcohol and 4 grams in those not taking alcohol.]

SUMMARY OF PRODUCT CHARACTERISTICS “It is indicated in mild to moderate pains such as headache, dental pain, acute migraine attacks, neuralgia, musculoskeletal system pains and dysmenorrhea and conditions accompanied by pain such as cold in adolescents aged 16 and above and adults. See section “4.4. Special warnings and precautions for use” of the product for children and adolescents.

PACKAGE LEAFLET “It is indicated in mild to moderate pains such as headache, dental pain, acute migraine attacks, neuralgia, musculoskeletal system pains and dysmenorrhea and conditions accompanied by pain such as cold in adolescents aged 16 and above and adults. See section “4.4. Special warnings and precautions for use of the product for children and adolescents.” 8- Only one of the following statements specific to the product should be written in addition to “It should not be used without the physician’s recommendation in children” in the part on children in section 4.4. Special warnings and precautions for use in the SPC of the products: - In combination products containing ASA: “Its use is not recommended under the age of 16 years unless there is a specific indication.” - In products containing only ASA: “Its use is not recommended under the age of 16 years unless there is a specific indication (such as Kawasaki disease).” 9-All statements related to indications, posology, warnings-precautions within the scope of this announcement should be adequately reflected in the Package Leaflet as well. I hereby submit for your information and kindly request that the SPC/PL applications in which the abovementioned amendments are made are sent to the Pharmacological Evaluation Unit until 31.01.2020 for review. Dr. Hakkı GÜRSÖZ President of the Agency

Distribution: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association Association of Innovator Pharmaceutical Companies Self-Care Products Association

REVOKED MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey Outgoing Document Service Outgoing Document No: 117489 Outgoing Document Date: 30.09.2014 Security Code: 868882 Procedure Tracking No: 1445084

Number : 77893119 Subject : Preparations Containing Acetyl Salicylic Acid

DOSSIER

The decision on the preparations containing Acetylsalicylic acid, declared to associations with the letter dated 07.08.2014, with No. 95839, has been updated as follows in line with the evaluation made by the "Advisory Commission on the Registration of Medicinal Products for Human Use". As per the decision adopted. - The preparations containing 300 mg and less acetylsalicylic acid will be regarded as non- prescription medicines, - The preparations containing 300 mg and more acetylsalicylic acid will be regarded as prescription medicines, - The preparations with indication for use in the pediatric population will be regarded as prescription medicines, - The preparations with indication for use in cardiovascular use will be regarded as prescription medicines, - In the preparations containing acetylsalicylic acid in combination with one or multiple active substances, evaluation will be made on a product basis to determine whether it is prescription/non-prescription (based on the active substance(s) with which it is combined, formulation, pharmaceutical form, etc.).

I hereby submit for your information and kindly request for the adoption of relevant action so that the member companies of your Association are duly informed on the abovementioned matters in their registration, SPC/PL, and package application made/to be made to us, and that the registration holders of the "Preparations Containing Acetyl Salicylic Acid" apply to the relevant units along with the SPC/PL and package samples in which abovementioned requirements are fulfilled until 14.11.2014.

Dr. Hakkı GÜRSÖZ Acting President of the Agency

Distribution for the conduct of relevant action: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association Association of Innovator Pharmaceutical Companies Self-Care Products Association

REVOKED MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey Outgoing Document Service Outgoing Document No: 95839 Outgoing Document Date: 07.08.2014 Security Code: 976829 Procedure Tracking No: 1391881

Number : 77893119 Subject : Preparations Containing Acetyl Salicylic Acid

DOSSIER

In line with the decision adopted by the "Advisory Commission on the Registration of Medicinal Products for Human Use" of our Agency on the preparations containing Acetylsalicylic acid, it has been deemed suitable to accept as non-prescription medicine the preparations containing 300 mg and less of acetylsalicylic acid alone or in combination with other active substances and to accept as prescription medicine the preparations containing the referred active substances at a dose of 300 mg and above.

I hereby submit for your information and kindly request for the adoption of relevant action so that the member companies of your Association are duly informed on the abovementioned matters in their registration, SPC/PL, and package applications made/to be made to use, and that the registration holders of the "Preparations Containing Acetyl Salicylic Acid" apply to the relevant unit along with the SPC/PL and package samples in which abovementioned requirements are fulfilled until 30.09.2014.

Dr. Saim KERMAN President of the Agency

Distribution for the conduct of relevant action: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association Association of Innovator Pharmaceutical Companies Self-Care Products Association

REVOKED MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY General Directorate of Pharmaceuticals and Pharmacy Ministry of Health of the Republic of Turkey Directorate General of Medicines and Pharmacy Documentation and Correspondence Branch-Outgoing Documents Service Date: 06.02.2021 Document No: 0012552 007007549646 Job Tracking No: 549646 Document Annex:

Number : B.10.0.IEG.0.10.00.03 Subject : Preparations containing acetylsalicylic acid

DOSSIER

In line with the decision adopted by the "Advisory Commission on the Registration of Medicinal Products for Human Use" of our Ministry on the preparations containing (alone or in combination) the active substance Acetylsalicylic acid (ASA), it has been deemed suitable to arrange as follows the indications section of the preparations containing the referred active substance.

ASA (at doses less than 500 mg) + Paracetamol + Caffeine It is indicated for mild to moderate acute pain and febrile conditions in adolescents aged above 16 years and adults.

ASA (at doses less than 500 mg) + Ascorbic acid (Vitamin C) or Citric acid It is indicated for mild to moderate acute pain and febrile conditions in adolescents aged above 16 years and adults.

ASA (500 mg) It is indicated for mild to moderate acute pain and febrile conditions in adolescents aged above 16 years and adults. It is indicated in the treatment of inflammatory rheumatoid diseases.

ASA (500 mg) + Caffeine It is indicated for mild to moderate acute pain and febrile conditions in adults.

ASA + Pseudoephedrine It is indicated in case of mild to moderate acute febrile conditions accompanied by nasal congestion in adolescents aged 16 years and above and adults.

ASA (100 mg) It is indicated in mild to moderate acute pain and febrile conditions.

It is indicated in the treatment of inflammatory rheumatoid diseases.

It is indicated as an anti-thrombotic; in non-stable angina pectoris and the prevention of coronary thrombosis patients under risk (hypertensive, hyperlipidemic, diabetic patients); in the prophylaxis of myocardial reinfarction; in the prevention of postoperative thrombosis and embolism especially in by-pass and arteriovenous shunts in cardiovascular surgery; in transient ischemic attacks and prophylaxis of stroke.

Furthermore, it is deemed suitable to include the statement reading, "It should not be used in children without the recommendation of a doctor." In the Warnings/Precautions section.

ASA (300 mg) It is indicated in mild to moderate acute pain and febrile conditions.

It is indicated in the treatment of inflammatory rheumatoid diseases. It is indicated as an anti-thrombotic; in the inflammation of superficial veins, in non-stable angina pectoris and the prevention of coronary thrombosis in patients under risk (hypertensive, hyperlipidemic, diabetic patients); in the prophylaxis of myocardial reinfarction; in the prevention of postoperative thrombosis and embolism especially in by-pass and arteriovenous shunts in cardiovascular surgery; in transient ischemic attacks and prophylaxis of stroke.

Furthermore, it is deemed suitable to include the statement reading, "It should not be used in children without the recommendation of a doctor." in the Warnings/Precautions section.

I kindly request for submission of information to the relevant members of your Association regarding the abovementioned matters in the SPC/PL applications made/to be made to us.

Dr. Saim KERMAN President of the Agency

Distribution for the conduct of relevant action: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish

Pharmaceutical Industry Association Association of Innovator Pharmaceutical Companies
REVOKED MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY General Directorate of
Pharmaceuticals and Pharmacy
Number : B.10.0.IEG.0.10.000.02-P Subject : Acetyl Salicylic Acid Preparations

DOSSIER

In line with the decision adopted by the “Advisory Commission on the Registration of Medicinal Products for Human Use” of our Ministry on the preparations containing “Acetyl Salicylic Acid 0.5 g”, it is necessary to carry out the following.

It is deemed suitable to arrange the indications of the referred preparations as “It is used in the symptomatic treatment of mild-moderate pain and fever”. Furthermore, it is deemed suitable to include the statement reading “It should not be used in children outside the recommendation of a doctor” in the “Warnings/Precautions” section of the package leaflet or the relevant sections of the SPC/Package Leaflet. It is necessary to submit to us samples of the package leaflet, Summary of Product Characteristics/Package Leaflet prepared in line with this decision until 08.05.2009.

I hereby submit for your information and kindly request for the conduct of relevant action for the provision of information to the member companies of your Association regarding this matter.

Dr. Mahmut TOKAÇ on behalf of the Minister General Director

Distribution: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association

REVOKED MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY General Directorate of Pharmaceuticals and Pharmacy

Number : B.10.0.IEG.0.10.000.02-P Subject : Preparations Containing the Combination of Acetyl Salicylic Acid and Ascorbic Acid

DOSSIER

In line with the decision adopted by the “Advisory Commission on the Registration of Medicinal Products for Human Use” of our Ministry on the preparations in effervescent form containing the combination Acetylsalicylic acid and ascorbic acid, it is necessary to include only “Analgesic and antipyretic” indications in the “Indications” section of the package leaflets of the preparations in effervescent form containing less than 500 mg of acetylsalicylic acid and ascorbic acid.

I hereby submit for your information and kindly request for the conduct of relevant action for the provision of information to the member companies of your Association on the submission of three package leaflet samples prepared within this framework to us until 01.09.2007 for review.

Dr. Mahmut TOKAÇ on behalf of the Minister General Director

Distribution: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association

July 19, 2007