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Datasheet for the decision of 21 April 2026

Case Number: T 0594/24 - 3.3.07

Application Number: 09817723.1

Publication Number: 2345410

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Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL COMPOSITION FOR MODIFIED RELEASE

Patent Proprietor:
Astellas Pharma Inc.

Opponents:
Sandoz AG
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Hamm&Wittkopp Patentanwälte PartmbB
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Teva Pharmaceutical Industries Ltd
Brand Murray Fuller LLP
DEVA HOLDING ANONIM SIRKETI

Headword:
Pharmaceutical composition for modified-release/ASTELLAS

Relevant legal provisions:
RPBA 2020 Art. 12(4), 12(6) sentence 2, 13(2)
EPC Art. 100(a), 56

Keyword:
Amendment to case - (no)
Late-filed new submissions - admitted (no)
Admittance of late-filed evidences
Grounds for opposition - lack of inventive step (yes)

Decisions cited:
T 0197/86, T 0326/15

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Case Number: T 0594/24 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 21 April 2026

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Party as of right: (Intervenor 7)	DEVA HOLDING ANONIM SIRKETI HALKALI MERKEZ MAH BASIN EKSPRES CAD NO 1 34303 KUCUKCEKMECE ISTANBUL (TR)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted/electronically transmitted on 19 March 2024 rejecting the opposition filed against European patent No. 2345410 pursuant to Articl e 101(2) EPC.**

Composition of the Board:

Chairman D. Boulois
Members: J. Lécaillon
S. Ruhwinkel

Summary of Facts and Submissions

I. European patent 2 345 410 (hereinafter "the patent") was granted on the basis of 14 claims. The independent claim of the patent as granted read as follows:

"1. A pharmaceutical composition for modified-release, comprising (1) (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetic acid anilide, or a pharmaceutically acceptable salt thereof, (2) at least one additive which ensures penetration of water into the pharmaceutical composition and which has a solubility such that the volume of water required for dissolving 1 g of the additive is 10 mL or less, and (3) a hydrogel-forming polymer having an average molecular weight of 100,000 to 5,000,000 or a viscosity of 12 mPa.s or more in a 5% aqueous solution at 25°C and 7,500 mPa.s or less in a 1% aqueous solution at 25°C,
wherein the additive which ensures penetration of water into the pharmaceutical composition is one compound, or two or more compounds selected from the group consisting of polyethylene glycol, polyvinylpyrrolidone, D-mannitol, lactose, sucrose, sodium chloride, and polyoxyethylene polyoxypropylene glycol;
wherein the hydrogel-forming polymer is one compound, or two or more compounds selected from the group consisting of polyethylene oxide, hydroxypropyl methylcellulose, and hydroxypropyl cellulose; and
wherein the drug dissolution rate from the pharmaceutical composition is 75% or less after 1.5 hours and at least 75% after 7 hours from the beginning of the dissolution test and wherein the dissolution test is carried out in accordance with the paddle

method described in the United States Pharmacopoeia under the conditions that 900 ml of USP buffer, pH 6.8, is used and the paddle rotation speed is 50 to 200 rpm."

II. Six oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application as originally filed.

III. The opposition division took the decision to reject the oppositions.

IV. The decision of the opposition division, posted on 19 March 2024, cited *inter alia* the following documents:

D3a: EP 1 559 427 A1
D4: WO 94/06414 A1
D7a: EP 2 119 442 A1
D8: Letter of the then-applicant in the examination proceedings dated 13 March 2020
D11: Clinical Pharmacology and Biopharmaceutics Review for mirabegron by the FDA, 7 March 2012
D19: EP 2 554 168 A1
D20: FDA’s Guidance for Industry - Food-Effect Bioavailability and Fed Bioequivalence Studies, December 2002
D48: EP 1 529 526 A1
D55: Atul Tiwari and Krishna S Naruganhalli, Expert. Opin. Invest. Drugs, 2006, 15(9), 1017-1037
D56: Martin C. Michel, *et al.*, Eur Urol Suppl 4, February 2005, 15-24, including front cover and contents
D58: Yamanouchi Press Release 11 May 1999

D59: Yamanouchi Press Release 27 September 2004, last updated 19 July 2008
D74: Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, page 1 and 11 to 15
D80: J.A. Fix *et al.*, "Controlled-Release Oral Delivery Systems" - Chapter 2 of "Controlling Drug Delivery - Designing Technologies for the Future", K. Park and R.J. Mrsny, ACS Symposium Series, Washington DC, 2000
D99: Archive of http://www.imagesrising.com/ypt/ocas.shtml as of 7 August 2008.

V. The opposition division decided in particular as follows:

(a) The subject-matter of granted claim 1 was originally directly and unambiguously disclosed.

(b) The claimed subject-matter was sufficiently disclosed.

(c) The claimed subject-matter was novel over D3/D3a. Furthermore the clinical trials with mirabegron did not represent a public prior use of tablets according to the present claims. The granted claims were therefore novel.

(d) The claimed subject-matter involved an inventive step starting from D3a as closest prior art. The claimed subject-matter differed from the one of D3a in that the drug dissolution rate of the tablet was lower. The reduction of a food effect observed for a conventional immediate-release formulation of mirabegron had not been convincingly substantiated. The objective technical problem resided

consequently in the provision of an alternative composition of mirabegron. Since there was no pointer in D3a to investigate the food effect, there would have been no incentive for the skilled person to combine the teaching of D3a with any one of D4, D7a, D48, D56/D59, D58, D80 or D99. Furthermore, none of the cited documents suggested the claimed dissolution rate.

VI. Opponents 1 to 6 (appellants 1 to 6) lodged appeals against the above decision of the opposition division.

VII. With their reply to the appellants' statement setting out the grounds of appeal the patent proprietor (respondent) defended their case on the basis of the patent as granted as the main request, and on the basis of 20 auxiliary requests filed therewith.

VIII. A notice of intervention was filed on 29 January 2026. The respondent filed a reply to the notice of intervention on 1 April 2026 and maintained the previous requests.

IX. The following items of evidence were filed by the parties during the appeal proceedings:

(a) Documents filed by appellant 3 with their statement setting out the grounds of appeal:

D135: A.G. Thombre, Drug Discovery Today, Sept 2005, 10(17), 1159-1166
D136: B. Myers Davit and D.P. Conner, Biopharmaceutics Applications in Drug Development – Chapter 10, 26 November 2007, 317-335

(b) Documents filed by the intervener with their notice of intervention (D137 to D147) and with their letters of 13 April 2026 (D151 to D155) and 16 April 2026 (D156):

D137: EMEA, Note for guidance on modified-release oral and transdermal dosage forms: Section II (Pharmacokinetic and clinical evaluation), 28 July 1999, 1-11
D138: Chen *et al.*, Pharmaceutical Research, Vol. 24, No. 1, January 2007, 73-80
D139: Ruis-Picazo *et al.*, Expert Opinion on Drug Delivery, 26 August 2020, DOI:10.1080/17425247.202.1813108
D140: Ibrahim *et al.*, RSC Pharm., 2025, 2, 369-386
D141: Krishnan *et al.*, Journal of Polymer Science, Part A : Polymer Chemistry, 2014, 52, 1917-1928
D142: Y. Batyrbekov and R. Iskakov, Polyurethane, Chapter 8, 2012, 147-170
D143: Bhadra *et al.*, Pharmaceutical Technology, 2 April 2007, 31(4), 1-17
D144: Kacar *et al.*, J. Coat. Technol. Res., 2018, DOI: 10.1007/s11998-018-0065 -4
D145: Adam Stoklosa, Thesis, "Water-Solid Interactions: Crystalline Powder Characterization and Development of Atomic Force Microscopy Techniques", May 2009
D146: Yué Bi Yao Clément, IJSRM, Vol. 06, 4, April 2018, FT 2018-01-09
D147: Shah *et al.*, International Journal of Pharmaceutical Sciences and Drug Research, 2014, 6(2), 95-101

D151: Silva *et al.*, Journal of Colloid and Interface Science 317, 2008, 333-340
D152: Cremer *et al.*, Heliyon, 9, 2023, e13604

D153: M. Martin-Pastor and E. Stoyanov, Journal of Polymer Science, 2020, 58, 1632-1641
D154: Chang and Robinson, Pharmaceutical Dosage Forms: Tablets, Volume 3, 2nd Edition, 27 July 1990, 238-239
D155: D.A. Alderman, International Journal of Pharmaceutics and Technology Production Manufacturing, Vol 5, No. 3, 1984, 1-9

D156: Colin D. Melia, Critical Reviews in Therapeutic Drug Carrier Systems, 1991, 8(4), 395-421

(c) Documents filed by the respondent with their reply to the notice of intervention on 1 April 2026:

D148: Catalogue Entry, IFF - ChemPoint, POLYOX^{TM} WSR 303
D149: M. Rubinstein and R.H. Colby, Polymer Physics, "Contents" and pages 325-334
D150: EP 2 554 168 A1 (corresponds to D19 submitted during the opposition proceedings)

X. Oral proceedings were held before the Board on 21 April 2026. As announced with the letters dated 4 February 2026, 19 March 2026 and 20 April 2026, appellants 3 and 4 and the intervener did not attend the oral proceedings. During the oral proceedings, the respondent withdrew all their auxiliary requests.

XI. The appellants 1 to 6 and the intervener requested that the decision under appeal be set aside and that the patent be revoked.

Appellants 1 and 5 also requested that the submissions and experimental data filed by the respondent on pages

8 to 12 of the letter dated 1 April 2026 not be admitted into the appeal proceedings.

XII. The respondent requested that the appeal be dismissed and the patent be maintained as granted.

Furthermore, the respondent requested that
- documents D135 and D136,
- the submissions of appellant 1 by letter dated 13 April 2026,
- the new submissions and experimental data submitted by the intervener with letter dated 13 April 2026 and documents D151 to 156,
not be admitted into the appeal proceedings.

XIII. The arguments of the appellants and the intervener, as far as relevant for the present decision, can be summarised as follows:

(a) Admittance of late filed submissions

(i) Appellants 1 and 5 considered that pages 8 to 12 of the respondent's letter of 1 April 2026 contained new submissions and experimental data which represented amendments to the respondent's case. They were not to be admitted into the appeal proceedings pursuant to Article 13(2) RPBA because there were no exceptional circumstances justifying their late submissions.

(ii) Appellant 1 considered that the arguments provided in their letter of 13 April 2026 did not constitute amendments to their case

and were therefore not to be excluded from the appeal proceedings.

(iii) The intervener did not provide reasons for the admittance of their submissions dated 13 April 2026 and the documents D151 to D156 filed therewith.

(iv) Appellant 3 argued that D135 was filed with their statement of grounds of appeal in direct response to the impugned decision and should therefore be admitted into the appeal proceedings.

(v) Appellant 3 further explained that D136 was filed with their statement of grounds of appeal to provide further support for their opinion that the alleged technical effect of reduction of the food effect was not associated with the claimed dissolution profile. D136 was to be admitted into the appeal proceedings.

(b) Inventive step

The main request did not meet the requirements of Article 56 EPC.

D3a, example 4, represented a suitable starting point for the assessment of inventive step. The subject-matter of claim 1 of the main request differed from example 4 of D3a in the drug dissolution rate from the formulation.

The effect of reduction of the food effect with the claimed modified-release formulation compared to

immediate-release compositions had not been appropriately substantiated (i) as directly resulting from the claimed distinguishing feature over the closest prior art nor (ii) as occurring over the whole scope of claim 1.

The objective technical problem was thus to be formulated as:

- the provision of an alternative pharmaceutical composition of mirabegron (as done by appellants 1 to 3, and 5 to 6),
- the provision of an alternative formulation of mirabegron which provided slower release (as done by appellant 4), or
- the provision of an alternative modified-release formulation (as done by the intervener).

The solution provided in claim 1 of the main request was obvious. The provision of modified-release formulations for the treatment of overactive bladder was known from the prior art (see *e.g.* D55). Furthermore, the oral controlled absorption system (OCAS) technology was known for the preparation of modified-release formulations. Hence, the claimed dissolution rate represented merely an arbitrarily selected feature within the routine work of the skilled person.

Moreover, even if the objective technical problem would be formulated in a more ambitious manner by including the reduction of the food effect, the claimed subject-matter would nevertheless be obvious. The skilled person would have routinely investigated the food effect for conventional formulations (see D20) and hence be aware of this issue. Furthermore, the OCAS technology was well-

known and described as reducing the food effect (see D80 and D58).

XIV. The arguments of the respondent, as far as relevant for the present decision, can be summarised as follows:

(a) Admittance of late filed submissions

(i) The arguments and experimental data included in the letter of 1 April 2026 were to be admitted into the appeal proceedings. The submissions included in said letter were made in direct response to the notice of intervention, which represented exceptional circumstances. Furthermore, the presented experimental data originated mainly from D19 and the granted patent and merely some data points were added. They did therefore not represent amendments to their case.

(ii) The submissions of appellant 1 filed on 13 April 2026 should not be admitted into the appeal proceedings because they were very late filed and there were no exceptional circumstances justifying their filing at that stage of the proceedings.

(iii) The submissions of the intervener filed on 13 April 2026 and the documents D151 to D156 submitted therewith should not be admitted into the appeal proceedings because they were very late filed and raised new points. There were furthermore no exceptional circumstances justifying

their filing at that stage of the proceedings.

(iv) D135 should not be admitted into the appeal proceedings, since it was not suitable to address the issue which led to the impugned decision.

(v) D136 was not to be admitted into the appeal proceedings. It should have already been filed with the opposition writ of appellant 3, in which the issue of reduction of the food effect not being associated with the claimed dissolution profile was already raised.

(b) Inventive step

The main request fulfilled the requirements of Article 56 EPC.

D3a, example 4, represented a suitable starting point for the assessment of inventive step. The subject-matter of claim 1 of the main request differed from example 4 of D3a in the drug dissolution rate from the formulation.

The patent identified, for the first time, a food effect associated with immediate-release mirabegron formulations and taught that this effect depended solely on the *in vivo* drug release rate, which was directly correlated to the claimed *in vitro* dissolution rate. On that basis, the comparison provided in the patent between the formulation according to claim 1 (example 8) and an immediate-release formulation (comparative example 1) was

generally applicable, *i.e.* that the observed reduction of food effect applied over any immediate-release formulation, hence including the formulation of example 4 of the closest prior art D3a.

The objective technical problem resided consequently in the provision of an improved formulation with reduced food effect.

The solution provided in claim 1 of the main request was not obvious, since there was no teaching or suggestion in the prior art that a mirabegron formulation achieving the claimed dissolution profile reduced the food effect. The issue of food effect with mirabegron conventional (immediate-release) formulations was not known. The investigation thereof mentioned in D20 was merely a recommendation and no obligation. Furthermore, none of the combination documents referred to by the appellants and the intervener disclosed the presently claimed dissolution profile. In particular, as explained in D80, the OCAS technology aimed at targeting delivery of the drug to the colon, which was not recommended for mirabegron and furthermore implied a slower release rate and hence a different dissolution rate. The claimed dissolution rate was not arbitrary. The lower limit excluded immediate-release formulations ensuring the reduction of the food effect and the upper limit provided the effect of ensuring satisfactory therapeutic efficacy.

Reasons for the Decision

1. Admittance of submissions and items of evidence

1.1 Submissions and experimental data filed by the respondent on pages 8 to 12 of the letter dated 1 April 2026

1.1.1 According to appellants 1 and 5, pages 8 to 12 of the respondent's letter of 1 April 2026 contained new submissions and experimental data which represented amendments to the respondent's case. Appellants 1 and 5 requested them not to be admitted into the appeal proceedings pursuant to Article 13(2) RPBA because there were no exceptional circumstances justifying their late submissions.

1.1.2 In the respondent's view, these submissions were made in direct response to the notice of intervention, which represents exceptional circumstances. In particular, they addressed the argument of the intervener that there would not be any technical relationship between the various features of claim 1 of the main request (see notice of intervention, page 22, last paragraph before point 4.1.2). Furthermore, the data originated mainly from D19 and the granted patent and merely some data points were added. These submissions did therefore not represent amendments to their case.

1.1.3 The Board observes that the following parts of the respondent's letter of 1 April 2026 are indeed newly filed or contain data newly compiled and hence represent amendments to the respondent's case:

- page 8, starting from "Upon discovery..." to page 10, line 3 (newly submitted data),

- page 10, the last paragraph starting from "In terms of data points..." to the first table on the top of page 11 (data newly put together from D19 and the patent as granted; data for the "IR Tablet" are newly submitted), and
- the table on page 12 (newly submitted data) and the related arguments.

1.1.4 These amendments address issues relevant for the assessment of inventive step, which were already raised in the notices of opposition and the impugned decision (see *e.g.* paragraph 23.2). In particular the issue of which factor is rate-limiting in the drug absorption and of an effect linked to the claimed dissolution rate were already raised during the opposition proceedings and reiterated at the onset of the appeal proceedings (see *e.g.* statement of grounds of appeal of appellant 5, paragraphs 106 and 110) and subsequently in the communication according to Article 15(1) RPBA of the Board (see paragraph 6.3).

Contrary to the respondent's view, the notice of intervention did not raise in this context any new point that would justify the filing of these new data and the related arguments. These amendments do therefore not represent a direct response to any new objection raised in the notice of intervention.

There were therefore no exceptional circumstances justified by cogent reasons for submitting these amendments at this late stage of the appeal proceedings.

1.1.5 Accordingly, the Board does not admit the above identified parts of the respondent's letter of 1 April

2026 (see point 1.1.3) into the appeal proceedings (Article 13(2) RPBA).

1.2 Submissions of appellant 1 by letter dated 13 April 2026

1.2.1 The respondent requested that the submissions of appellant 1 filed on 13 April 2026 not be admitted into the appeal proceedings because they were very late filed and there were no exceptional circumstances justifying their filing at that stage of the proceedings.

1.2.2 The letter of 13 April 2026 contains only arguments which represent merely further developments of the already provided line of argument. They do therefore not constitute amendments to appellant 1's case. Hence, there are no reasons to exclude these submissions from the appeal proceedings.

1.2.3 As a result, the submissions by appellant 1 filed by letter dated 13 April 2026 are admitted into the appeal proceedings.

1.3 New submissions, experimental data and D151 to D156 submitted by the intervener with letter dated 13 April 2026

1.3.1 The respondent requested that the submissions of the intervener filed on 13 April 2026 and the documents D151 to D156 submitted therewith not be admitted into the appeal proceedings because they were very late filed and raised new points, such as the gelling behaviour of some polymers mentioned in the patent, and there were furthermore no exceptional circumstances

justifying their filing at that stage of the proceedings.

1.3.2 The intervener did not provide any argument in support of the admittance of their submission of 13 April 2026 and documents D151 to D156 filed therewith.

1.3.3 The Board observes that the point 3 and all submissions set out in points 4 and 5 relating to documents D151 to D156 and the gelling properties of HPC of the intervener's letter of 13 April 2026 are newly filed and represent indeed amendments to the intervener's case. These submissions as well as the supporting documents D151 to D156 filed with said letter raise entirely new issues. They do not represent a direct response to the respondent's reply to the notice of intervention nor to any new development of the present case.

There were therefore no exceptional circumstances justified by cogent reasons for submitting these amendments at this late stage of the appeal proceedings.

1.3.4 Accordingly, the Board does not admit:

- the intervener's submissions set out in point 3 of their letter dated 13 April 2026,
- all submissions set out in points 4 and 5 of said letter relating to documents D151 to D156 and the gelling properties of HPC, and
- D151 to D156,

into the appeal proceedings (Articles 13(2), 14 RPBA RPBA).

1.4 D135

1.4.1 According to appellant 3, this document was filed with their statement of grounds of appeal in direct response to the impugned decision. It aimed at providing evidence that an immediate-release formulation was given to the patients in the Blossom trial (D28).

1.4.2 As stated by the respondent, the review article D135 does not mention mirabegron or the Blossom trial. The Board further observes that the sentence cited by appellant 3 is very general. The mere fact that "controlled release formulations have generally been considered as follow-ons to conventional immediate-release formulations" cannot represent evidence of the type of formulation used in a specific clinical trial.

1.4.3 Accordingly, the Board considers that D135 does not provide the evidence requested by the opposition division and hence is not suitable to address the issue which led to the impugned decision.

1.4.4 The Board therefore does not admit D135 into the appeal proceedings (Article 12(4) RPBA).

1.5 D136

1.5.1 This document was filed by appellant 3 with their statement of grounds of appeal to provide further support for their opinion that the alleged technical effect of reduction of the food effect is not associated with the claimed dissolution profile. D136 is a chapter of a textbook dealing with food effects on drug bioavailability. The passages cited by appellant 3 concern the fact that one possibility of food to affect

drug bioavailability is by altering its release, in particular such as the phenomenon of dose dumping.

1.5.2 The respondent brought forward that this document should have already been filed with the opposition writ of appellant 3, in which the present issue was already raised.

1.5.3 The Board observes that, as underlined by the respondent, the argument that D136 is meant to support has been on file since the beginning of the opposition proceedings and does therefore not represent an amendment to appellant's 3 case. Furthermore, D136 represents evidence of common general knowledge on food effects on drug bioavailability in support of said argument and is not complex. Moreover, its filing with the statement of grounds of appeal is not prejudicial to procedural economy. Finally, the Board does not see any reasons which would have required the filing of D136 already in the opposition proceedings.

1.5.4 D136 is therefore admitted into the appeal proceedings (Articles 12(4) and 12(6), 2nd sentence RPBA).

Main request - Patent as granted

2. Inventive step

2.1 Closest prior art

2.1.1 All parties provided arguments starting from *inter alia* D3a as closest prior art in line with the impugned decision.

2.1.2 D3a discloses mirabegron for use in the treatment of overactive bladder (see paragraphs [0001], [0009] and

[0015]). A variety of dosage forms, including solid oral dosage forms (see *e.g.* paragraph [0017]), is described. A tablet containing excipients falling under the definition of present claim 1 is disclosed and represents the closest prior art embodiment (see page 9, example 4; table 5). This tablet contains lactose and polyethylene glycol 6000 (PEG 6000) as additives and hydroxypropyl cellulose (HPC) and hydroxypropyl methyl cellulose (HPMC) as hydrogel-forming polymers.

2.2 Distinguishing feature and associated technical effect

2.2.1 No drug dissolution rate is disclosed for the composition of example 4 of D3a. However, it was undisputed in the appeal proceedings that the experimental data provided by the respondent substantiate that this dosage form provides a rapid release (see D8, page 2, starting from "2 Novelty" to page 3, 1st paragraph). It was hence common ground that the claimed compositions differ from the one of example 4 of D3a in the drug dissolution rate from the tablet.

2.2.2 The respondent argued that the technical effect linked to the specific drug dissolution rate of claim 1 resided in a reduction of the food effect compared to immediate-release forms. The respondent relied on the experimental data provided for example 8 and comparative example 1 of the patent (see Tables 2 and 4 and paragraphs [0104] and [0112] of the patent).

2.2.3 As argued in the impugned decision as well as by the appellants, the compositions of example 8 and the comparative example 1 differ from each other not only in the *in vitro* drug dissolution rate but also in the nature of the dosage form (tablet versus capsule), the amount of drug and the nature and amount of excipients.

This comparison does therefore not fulfil the well-established requirement that the nature of the comparison must be such that the technical effect is convincingly shown to have its origin in the distinguishing feature (T 197/86, headnote).

The Board understands that, as argued by the respondent, modifications of the dosage form may be required in order to achieve different drug dissolution profiles. However, in the present case, the composition tested in the comparative example 1 is more remote from the composition of the invention than the tablets of the closest prior art. Furthermore, as revealed by D8, reproduction of the closest prior art tablets appears to have been possible.

2.2.4 The respondent argued that the patent (see paragraphs [0001], [0005], [0009] to [0012] and [0113]) identified for the first time a food effect with immediate-release formulations of mirabegron. The patent further provided a clear teaching that the observed food effect depended only on the absorption rate of mirabegron, which was directly correlated to the drug release rate. The patent hence taught that selecting an appropriate modified-release rate allowed to reduce said food effect. The desired release rate was directly correlated to the claimed dissolution rate and not determined by the excipients. The respondent concluded that the observed reduction of the food effect observed for the modified-release formulation of example 8 of the patent compared to the immediate-release formulation of comparative example 1 would be observed over any immediate-release formulation, *i.e.* also for the one of example 4 of D3a. The general consensus that immediate-release formulations were considered equivalent irrespective of the excipients used was

confirmed by D74 (Article 10(2)(b), "The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form").

Furthermore, D3a envisaged capsule formulations (see paragraph [0017]), so that the formulation of comparative example 1 of the patent was in accordance with the closest prior art.

Finally, D8 substantiated that the observed food effect was not affected by the drug dose (see last table on page 6).

2.2.5 These arguments are not convincing.

No experimental evidence nor exact definition of the alleged direct correlation between the *in vitro* dissolution rate of mirabegron as defined in the claims, its *in vivo* release rate and its absorption rate was provided. Furthermore, the respondent did also not provide any evidence in support of the allegation that amongst the features defining the formulations only the *in vitro* dissolution rate was responsible for the alleged effect and that further features had no impact thereupon. Moreover, as argued by appellants, there is no evidence that the claimed range of dissolution rates will necessarily result in a continuous drug release for 4 hours or more as defined in paragraph [0010] of the patent. The results obtained for the specific comparison of a formulation according to the invention (example 8 of the patent) with comparative example 1 of the patent cannot therefore be extrapolated for any immediate-release formulation, including the one of the closest prior art, nor over

the whole range of dissolution rates defined in claim 1 of the main request.

The reference of the respondent to D74 (EU guidelines for generic medications) concerns bioequivalence between a reference medicinal product and a generic form thereof and, as argued by appellant 5, does not relate to food effect. Hence, the citation of D74 cannot lead to the conclusion that the reduction of the food effect observed over the formulation of comparative example 1 would necessarily be obtained over any rapid-release formulation.

In this context, D3a's general reference to capsules as a suitable oral administration form does not affect the finding that example 4 constitutes the closest embodiment of D3a *i.e.* the appropriate starting point for the assessment of inventive step.

With regard to the respondent's argument concerning the difference in drug dose between the formulations of example 8 and of comparative example 1 of the patent, the Board observes that the results provided in the last table on page 6 of D8 for a specific modified-release formulation according to the invention do not preclude that the dosage could have an influence in the case of immediate-release formulations, *i.e.* for the formulation of comparative example 1.

2.3 Objective technical problem

2.3.1 It follows that the technical effect alleged by the respondent has not been substantiated as directly resulting from the distinguishing feature and as occurring over the whole scope claimed.

2.3.2 Accordingly, the Board considers that the alleged technical effect cannot be taken into account in the formulation of the objective technical problem, which can hence only be formulated as the provision of another pharmaceutical composition of mirabegron.

2.4 Obviousness

2.4.1 The preparation of a modified-release formulation instead of an immediate-release formulation in the case of an oral treatment of overactive bladder does not provide any inventive contribution over the closest prior art compositions. Modified release formulations formed part of the common general knowledge of a formulation chemist. In particular, as brought forward by appellant 5, such formulations allowing to reduce the frequency of administration (*e.g.* once daily administration) were commonly known as advantageous formulations in the treatment of overactive bladder (see *e.g.* the scientific review D55, Table 1 and page 1022, 1st full paragraph).

2.4.2 Furthermore, as mentioned by the appellants, methods of preparation of modified-release formulations containing the same type of excipients as the composition of example 4 of D3a were also commonly known in the art (see *e.g.* the OCAS technology disclosed *inter alia* in the textbook D80, see in particular Abstract and pages 19 to 20). The specific dissolution rate claimed, which is the sole distinguishing feature over the composition of example 4 of D3a taken as the closest prior art, represents an arbitrary choice falling within the routine activity of the skilled person in the art seeking to provide a modified-release formulation of mirabegron as a solution to the above-defined technical problem. No specific effect linked to the defined range

apart from excluding rapid-release formulations was substantiated. In particular, the alleged effect of the upper limit ("at least 75% after 7 hours") of ensuring satisfactory therapeutic efficacy has not been substantiated by the respondent.

2.4.3 Having regard to the arguments of the respondent and the reasoning of the opposition division relating to the non-obviousness of the reduction of the food effect, the Board reminds that, if the alleged technical effect is not considered to have been appropriately substantiated, it should not be taken into consideration in the assessment of obviousness either.

2.4.4 It follows that the mirabegron formulation of claim 1 of the main request would have been obvious to the skilled person willing to solve the above problem starting from example 4 of D3a in combination with the common general knowledge, including the known OCAS technology, as described in *e.g.* D80.

2.4.5 Finally, in response to the respondent's line of argument, the Board observes that, even if the alleged effect of reduced food effect had been credibly demonstrated for the claimed modified-release formulations vis-à-vis the rapid-release formulation of the closest prior art, and a more ambitious technical problem were to be formulated on that basis, the claimed subject-matter would nevertheless be obvious to the person skilled in the art.

As brought forward by appellant 1 with reference to D20 illustrating common general knowledge (see *e.g.* page 1, first paragraph under "Background") and in line with T 326/15 (see r. 1.10 and 1.11), a systematic

investigation of food effects represented a routine measure in the development of new medicines to optimise the bioavailability thereof. In particular, according to D20, a food-effect bioavailability study was recommended at an early stage of drug development for all new chemical entities formulated as immediate-release drug products (see page 3, first two paragraphs under III.A.1).

The Board therefore considers that, contrary to the respondent's view, the skilled person would necessarily have tested the mirabegron conventional (*i.e.* immediate-release) formulations for food-effect bioavailability. D20 also provides guidance for said evaluation (see page 4, part IV onwards) similar to the one performed in the granted patent (see paragraph [0005]). By doing so, the skilled person would have found that bioavailability of mirabegron is affected by the presence or absence of the intake of food. As mentioned by appellant 1, the post-published document D11 confirms that such studies were indeed routinely performed in the case of the development of mirabegron formulations (see pages 10 to 11, part 2.1.4.2.1).

As argued by the appellants, modified-release formulations according to the OCAS technology disclosed in D80, D48, D56, D58 or D59 represented an obvious measure to reduce the food effect in the development of drug formulations. The OCAS technology was known to be applicable in general independently of any specific active ingredient and to reduce food effects (see D80, Abstract and page 21, penultimate paragraph to page 23, first paragraph and D58, 3rd paragraph). Furthermore, this technology involved the use of a hydrogel-forming polymer and an additive in accordance with claim 1 of the main request, including PEG 6000 as additive and

polyethylene oxide, hydroxypropyl methylcellulose or hydroxypropyl cellulose as hydrogel-forming polymer used in the examples of the patent and in example 4 of the closest prior art D3a (see D80, pages 19 to 20). It follows that the preparation of a mirabegron modified-release formulation based on OCAS technology with the aim of reducing the food effect would have been obvious to the skilled person, who would thus have arrived at a formulation fulfilling the structural features of claim 1 of the main request.

Finally, the skilled person would consider the claimed *in vitro* dissolution rate to represent an arbitrary feature for the same reasons as detailed above under point 2.4.2.

As a result, the claimed formulation would also have represented an obvious solution to a technical problem taking into account a reduction of the food effect starting from example 4 of D3a in combination with the known OCAS technology, as described *e.g.* in D80.

The respondent argued that OCAS technology aimed at achieving drug delivery and absorption in the colon, which was not desirable for mirabegron. However, the respondent did not provide any evidence of the actual delivery site of mirabegron with the claimed modified-release formulations. In this context, the respondent referred to the calculated 4 hours window for *in vivo* release of mirabegron (see paragraph [0010] of the patent) which would correspond to a release in the small intestine. As already explained before (see point 2.2.5), the *in vivo* release rate is not claimed but the *in vitro* dissolution rate, and no direct correlation between them has been substantiated. Moreover, paragraph [0010] of the patent mentions a "continuous

drug release for 4 hours or more". There is therefore no evidence on file that mirabegron administered in the form of the claimed formulation will necessarily be released and/or absorbed before the colon. Furthermore, the Board observes that, according to D80, the purpose of the OCAS technology is to achieve full hydration in the small intestine and hence full release of the drug in the colon. As mentioned by appellant 5, (partial) release in small-intestine is also considered (see page 18, 1st full paragraph and Figure 4). This argument of the respondent is therefore not cogent.

2.5 As a result, the ground for opposition according to Article 100(a) EPC in combination with Article 56 EPC prejudices the maintenance of the patent as granted.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar: The Chairman:

C. Rodríguez Rodríguez D. Boulois

Decision electronically authenticated