



When »in combination with« is not so simple

Newron's SPC application for safinamide and Genmab's SPC applications for DARZALEX®

Loose combinations refer to treatment regimens where multiple active ingredients are administered together but are not contained in the same medicinal product e.g. for allowing for adjusting the dose of the both active ingredients. They represent a particular difficulty under the European supplementary protection certificate (SPC) Regulation¹. In such a situation, the patent may protect a therapeutic use involving two active ingredients, while the marketing authorization may formally cover a medicinal product containing only one of the two active ingredients.

¹ Regulation (EC) No 469/2009 of 6 May 2009

The loose-combination dilemma

This creates two imperfect routes to SPC protection. The applicant may seek an SPC for the authorized single active ingredient, in which case Article 3(b) of the Regulation may be satisfied, but Article 3(a) of the Regulation may be problematic if the patent is directed only to combination therapy. Alternatively, the applicant may seek an SPC for the combination of both active ingredients, in which case Article 3(a) of the Regulation may be easier to satisfy, but Article 3(b) of the Regulation becomes difficult if the marketing authorization formally relates to a medicinal product containing only one of the active ingredients.

This dilemma lies at the heart of recent disputes concerning loose combinations. The example of Newron's safinamide illustrates the »mono-product approach«: an SPC application for the single active ingredient, where the question was whether safinamide was protected by a patent claim referring to use »in combination with« levodopa/peripheral decarboxylase inhibitor (PDI). The SPC application was refused in several countries but was allowed on appeal by the German Federal Patent Court (BPatG, 14 W (pat) 23/24).

By contrast, the »combination-product approach« is the subject of the recent Court of Justice of the European Union (CJEU) referral in **Genmab/DARZALEX®**, Case C-262/26. This referral concerns the question whether a loose combination can itself be the »product« for SPC purposes where the marketing authorization and product information provide for combination use.

Legal background: the SPC requirements

The starting point for any SPC application in the European Union is Article 3 of Regulation (EC) No 469/2009. An SPC may be granted only if, in the Member State in which the application is filed and at the date of that application:

- (a) *the product is protected by a basic patent in force;*
- (b) *a valid marketing authorization has been granted for the product as a medicinal product;*
- (c) *the product has not already been the subject of an SPC;*
- and
- (d) *that authorization is the first authorization to place the product on the market as a medicinal product.*



For present purposes, the critical requirements are Articles 3(a) and 3(b) of the Regulation. Article 3(a) of the Regulation requires **the product** to be protected by a basic patent in force; Article 3(b) of the Regulation requires a valid marketing authorization to have been granted for **that product** as a medicinal product.

Article 1(b) of the Regulation defines the »product« as the active ingredient or combination of active ingredients of a medicinal product. **The Regulation does not, however, expressly state whether such a combination must be a fixed combination contained in a single medicinal product, typically in a fixed dosage ratio, or whether it may also include a loose combination, i.e., where the active ingredients are administered together but are contained in separate medicinal products.**

This ambiguity matters because Articles 3(a) and 3(b) of the Regulation must be satisfied for the same »product«.

In fixed-combination cases, the marketing authorization usually identifies both active ingredients. The »product« for SPC purposes will normally be the combination of active ingredients, and the assessment under Articles 3(a) and 3(b) of the Regulation is comparatively straightforward, provided the same combination is protected by the basic patent and covered by the marketing authorization.

In loose-combination cases, the product information for one medicinal product may, for example, state that it is »indicated in combination with« another medicinal product or active ingredient. The basic patent may protect the therapeutic combination, whereas the marketing authorization may formally relate only to one active ingredient. That possible mismatch underlies both the Newron safinamide case complex and the pending Genmab/DARZALEX® referral. These cases illustrate the resulting dilemma: whether the SPC product should be characterized as the authorized single active ingredient or as the therapeutic combination.

Previous case law

A central issue under Article 3(a) of the Regulation is how the protection conferred by the basic patent is to be assessed in relation to the relevant product. The CJEU case law distinguishes between two different situations: first, where the SPC is sought for a combination of active ingredients; and second, where the SPC is sought for one active ingredient although the patent claims that ingredient only as part of a combination.

SPC for a combination product: *Teva v. Gilead*

The first situation concerns an SPC application directed to a combination of active ingredients, where the question is whether that combination is protected by the basic patent.

In *Teva v. Gilead* (Case C-121/17), the CJEU adopted a two-step test for determining whether a combination product is »protected by a basic patent in force«. The assessment is made from the perspective of the skilled person and on the basis of the prior art at the filing or priority date of the patent:

- *»the combination of those active ingredients must necessarily, in the light of the description and drawings of that patent, fall under the invention covered by that patent« (item 57);*
- and*
- *»each of those active ingredients must be specifically identifiable, in the light of all the information disclosed by that patent.« (item 57)*

The *Teva v. Gilead* test was therefore mainly applied in the context of an SPC application for a combination of active ingredients. It addresses the question whether a combination, even if not expressly recited in the claims in that specific form, is nevertheless sufficiently disclosed and identifiable in the basic patent.

SPC for one active ingredient from a claimed combination

Medeva

The second situation was addressed in *Medeva* (Case C-322/10). Medeva's basic patent, EP 1 666 057, concerned a method for preparing a vaccine against *Bordetella pertussis*, the causative agent of whooping cough, and claimed a combination of two antigens as active ingredients, namely pertactin and filamentous haemagglutinin, in defined proportions so as to produce a synergistic effect in vaccine potency (Item 13 of *Medeva*).

The UK Patent Office refused Medeva's SPC applications on the ground that they specified active ingredients in addition to those identified in the claims of the basic patent, and those additional ingredients were therefore not protected by the basic patent within the meaning of Article 3(a) of the Regulation (Item 15 of *Medeva*).



Medeva appealed unsuccessfully to the High Court of Justice of England and Wales (Civil Division) and then to the Court of Appeal (England and Wales, Civil Division), which stayed the proceedings and referred questions to the CJEU. The referring court sought guidance on Article 3(a) of the Regulation, in particular on what is meant by »the product is protected by a basic patent in force« and on the criteria for determining this where the medicinal product comprises more than one active ingredient or is a multi-disease vaccine (Items 16 and 17 of Medeva).

The CJEU held, first, that Article 3(a) of the Regulation precludes the grant of an SPC *»relating to active ingredients which are not specified in the wording of the claims of the basic patent«*. In particular, *»if a patent claims that a product is composed of two active ingredients but does not make any claim in relation to one of those active ingredients individually, an SPC cannot be granted on the basis of such a patent for the one active ingredient considered in isolation«* (Items 25-28 of Medeva).

Secondly, the Court held that Article 3(b) of the Regulation does not preclude the grant of an SPC for a claimed combination of active ingredients merely because the underlying marketing authorization covers a medicinal product containing that combination together with other active ingredients, provided the other requirements of Article 3 of the Regulation are met (Items 29 and 42 of Medeva).

Yeda

Yeda Research (Case C-518/10) was the holder of EP0667 165, entitled »Therapeutic compositions containing monoclonal antibodies specific to the human epidermal growth factor (EGF) receptor«. The patent concerned therapeutic compositions comprising, first, a monoclonal antibody binding to the extracellular domain of the human EGF receptor and inhibiting tumor-cell growth (e.g. cetuximab) and, second, an anti-neoplastic agent (e.g., irinotecan) (Items 14 and 15 of Yeda).

The patent specifically stated that treatment with a combination of the antibody and an anti-neoplastic drug was more effective than using either component alone. The patent also specifically disclosed and claimed administration of both components separately, provided they are part of the same composition (Item 17 of Yeda).

Yeda Research filed two SPC applications: the first identified the product as »cetuximab in combination with irinotecan«, while the second identified only the active ingredient cetuximab (Yeda, para. 18). The UK Patent Office refused both SPC applications. The application for »cetuximab in combination with irinotecan« was refused because the marketing authorization covered cetuximab alone, such that Article 3(b) of the Regulation was not satisfied. The application for cetuximab alone was refused because, unlike the combination of cetuximab and irinotecan, cetuximab was not individually protected by the basic patent within the meaning of Article 3(a) of the Regulation (Item 23 of Yeda).



Yeda Research appealed the UK Patent Office's refusal before the High Court of Justice of England and Wales, which dismissed the action. Yeda Research then appealed to the Court of Appeal (England and Wales) (Civil Division) as regards the refusal of the SPC for cetuximab alone (Yeda, paras. 24 and 27). The case was referred by the Court of Appeal (England and Wales) (Civil Division) to the CJEU because Yeda Research argued that use of cetuximab alone would amount to »indirect or contributory infringement« and therefore should be treated as protected by the basic patent (items 27, 29 of Yeda).

The CJEU noted that the question referred was, »for all essential purposes, similar« to the questions in **Medeva**, and that the answers and clarifications given in **Medeva** were »equally valid« in **Yeda** (Items 31-32 of Yeda). It held that Article 3(a) of the Regulation precludes the grant of an SPC where the active ingredient, although »identified in the wording of the claims of the basic patent as an active ingredient forming part of a combination in conjunction with another active ingredient«, is »not the subject of any claim relating to that active ingredient alone« (Items 33, 39 and operative part of Yeda).

The mono-product route: Newron and safinamide

The safinamide case: Newron

Newron applied for SPCs in several European countries based on EP 1 613 296 and the EU marketing authorization for XADAGO® (EU/1/14/984) (safinamide). The patent includes an independent Swiss-type claim. Claim 1 specifies:

»The use of a first agent selected from safinamide from 0.5 to 1, 2, 3, 4 or 5 mg/kg/day in combination with levodopa/PDI, for the preparation of a medicament as a combined product for simultaneous, separated or sequential use for the treatment of Parkinson's Disease.«

In Germany, the German Patent and Trade Mark Office refused the application on a strict reading of **Yeda**. It considered that claims 1, 6, and 7 of the basic patent protected a combination of safinamide and levodopa/PDI, but not safinamide as a single active ingredient. Since the patent contained no claim directed to safinamide in isolation, while the XADAGO® marketing authorization concerned safinamide alone, the German Patent and Trade Mark Office decided that Article 3(a) of the Regulation was not satisfied (BPatG, 14 W (pat) 23/24, Reasons I, p. 3).

The German Federal Patent Court disagreed. It allowed the appeal, set aside the German Patent and Trade Mark Office's refusal, and granted an SPC (BPatG, 14 W (pat) 23/24, Reasons II, 18-19).

A central part of the German Federal Patent Court's reasoning was the distinction between different categories of claimed subject matter in EP 1 613 296:

1. *a pharmaceutical composition comprising safinamide and levodopa/PDI, as claimed in claim 7;*
2. *a kit comprising a safinamide composition and a levodopa/PDI composition, as claimed in claim and*
3. *the therapeutic use of safinamide for preparation of a medicament as a combined product, as claimed in claim 1, a Swiss-type claim.*

In the German Federal Patent Court's view, claim 1 was not directed to a fixed active-ingredient combination as such. Rather, it concerned the use of safinamide in a specific therapeutic context, namely as an add-on treatment in combination with levodopa/PDI for Parkinson's disease (Reasons II, 8). The German Federal Patent Court relied in particular on the wording of claim 1, which refers to the use of a »first agent selected from safinamide« and allows for »simultaneous, separated or sequential use«. According to the German Federal Patent Court, this showed that claim 1 did not necessarily require a single pharmaceutical composition containing both active ingredients, in contrast to claim 7 (Reasons II, 9).

The German Federal Patent Court further emphasized that a use claim may in principle serve as the basic patent for an SPC (Reasons II, 11). Applying the **Teva v. Gilead** test, it found that both requirements were satisfied: safinamide necessarily formed part of the invention disclosed in the patent, and safinamide was expressly named in claim 1 and was therefore specifically identifiable (Reasons II, 12).

As regards **Yeda**, the German Federal Patent Court held that the decision was not transferable. In **Yeda**, the relevant patent claim was directed to an active-ingredient composition. By contrast, in the safinamide case, claim 1 was interpreted as a use claim directed to safinamide in a combination therapy, not as a claim to an active-ingredient composition (Reasons II, 16).



Practical significance

The German Federal Patent Court's **Newron** decision shows that, in exceptional cases, there may be a possible path for SPC protection where the marketing authorization is for a single active ingredient but the basic patent refers to combination therapy.

However, this position remains uncertain. As in Germany, the Netherlands has granted an SPC for safinamide. In Germany, however, a nullity action against the SPC was filed before the German Federal Patent Court on 7 July 2026 (Case no. 3 Ni 10/26), shortly after its grant on 30 May 2026. The outcome of this nullity action may therefore have a significant bearing on the validity and enforceability of the German SPC.

The case highlights a structural feature of the SPC system: despite reliance on the same European basic patent and marketing authorization, SPC protection remains national, and national authorities and courts may reach different conclusions on the requirements for protection.

The combination-product route: Genmab/DARZALEX® Referral

The pending CJEU referral in **Genmab/DARZALEX®** (Case C-262/26) concerns the other side of the loose-combination dilemma.

Instead of asking whether the single active ingredient is protected by a basic patent directed to combination therapy, the **Genmab** case asks whether an SPC can be granted for the combination itself where the authorized medicinal product contains only one of the active ingredients, but its product information provides for use in combination with another medicinal product.

In other words, the issue is mainly focused on Article 3(b) of the Regulation:

Can a marketing authorization for a medicinal product containing active ingredient A satisfy Article 3(b) of the Regulation for an SPC directed to the combination of active ingredients A and B, where the product information indicates that A is to be used in combination with B?

This is a highly significant question. If the answer is yes, SPC protection for loose combinations may become possible in circumstances where it has often been refused in the past.

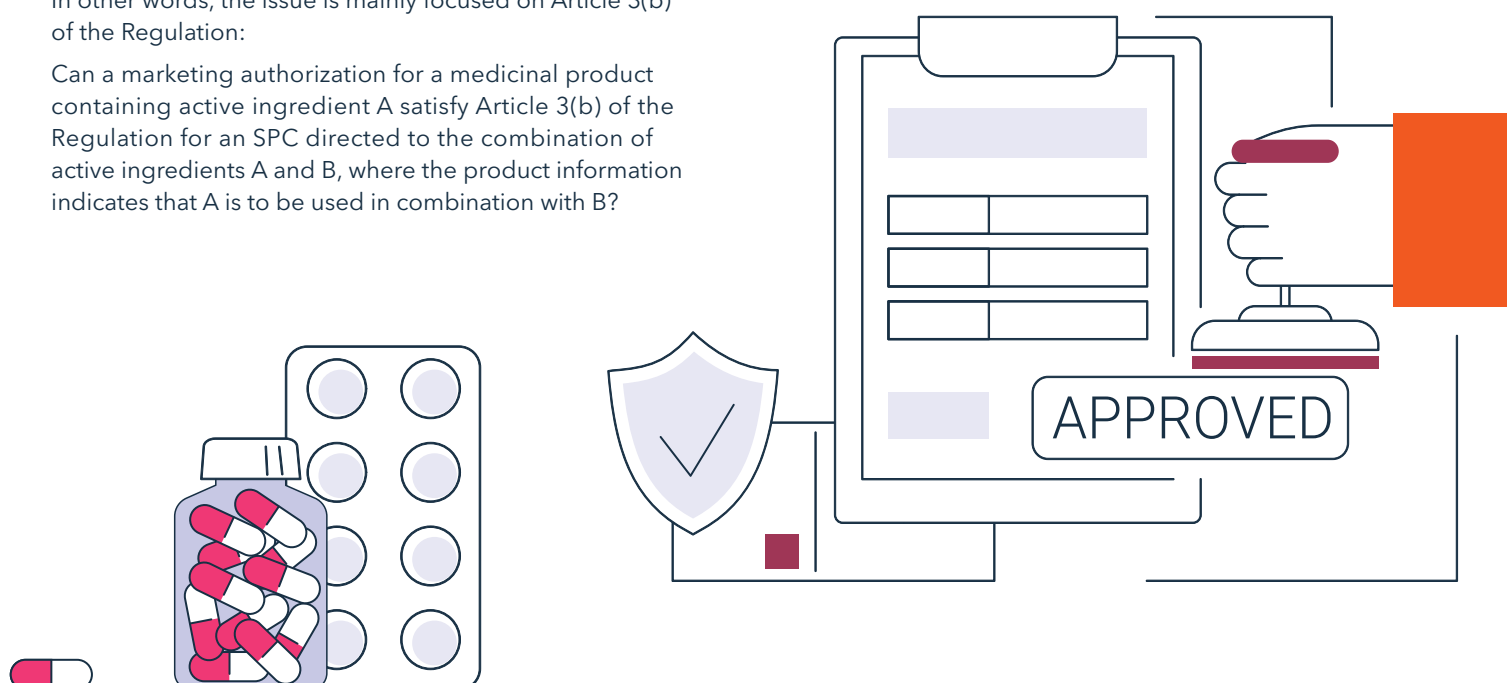
Genmab's DARZALEX® applications

The referral arises from Genmab's attempts to obtain SPC protection for loose combinations involving daratumumab, marketed as DARZALEX®.

Daratumumab was first authorized by the European Medicines Agency in 2016 as a monotherapy. Later, the authorization was amended through several Type-II variations to include combination uses with other active ingredients.

Genmab filed SPC applications for various loose combinations including daratumumab, relying on these Type-II variations and on EP 2 081 595 as the basic patent. Genmab is also the holder of an earlier patent, EP 2 567 976, which protects daratumumab as such. By contrast, the basic patent was granted and protects specific combination products, including the combination product in question, namely daratumumab, bortezomib, thalidomide, and dexamethasone.

The national outcomes have not been uniform: Some patent offices granted SPCs for the relevant loose combinations, e.g., Switzerland, Slovenia and Greece. Others, including offices in countries such as France and the Netherlands, refused them on the basis that Article 3(b) of the Regulation was not satisfied.



The Danish court referred questions to the CJEU to clarify whether SPC protection can be available for loose combinations.

In substance, the questions ask:

1. *Are Articles 1(b) and 3(b) of the Regulation to be interpreted as allowing an SPC for a product consisting of a new combination of active ingredients, where that combination has been authorized for combined use, even though the active ingredients are not present in the same pharmaceutical formulation but are administered separately as a loose combination?*
2. *If the answer to the first question is yes, can a Type-II variation of a marketing authorization for a new loose combination satisfy Article 3(b) of the Regulation, where the active ingredients are administered separately and are not contained in the same pharmaceutical formulation?*

Potential impact of the Genmab referral

If the CJEU answers the first question in the affirmative, it may open the door to SPC protection for loose combinations in the EU.

However, if the Court answers the questions negatively, the current restrictive approach is likely to continue. In that case, an SPC for a loose combination would remain difficult to obtain where the marketing authorization formally concerns only one active ingredient.

The pending CJEU **Genmab** referral may clarify whether the European SPC system can accommodate loose-combination therapies, or whether protection remains largely confined to fixed combinations and clearly authorized single active ingredients.

Conclusion

Newron and Genmab illustrate the two possible routes for loose-combination SPCs. In Newron, the applicant sought protection for the authorized single active ingredient and relied on a patent claim referring to combination therapy. In Genmab, the issue is whether the combination itself can be the SPC »product« where the marketing authorization and product information provide for combined use.

Both cases reflect the same structural problem: Articles 3(a) and 3(b) of the Regulation must be satisfied for the same »product«, but in loose-combination cases the basic patent and the marketing authorization may point to different products. The pending Genmab referral may therefore be important in determining whether EU SPC law can accommodate loose combinations beyond fixed-dose combinations and straightforward mono-product cases.



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