ENLI's Guide
on Pre-launch

NB! You can search in the Guide by pressing "Ctrl + F" and enter your keyword.

Index

1. General comments on Pre-launch

Medicines that are not approved for the Danish market must not be mentioned or otherwise used in a pharmaceutical advertising to Danish healthcare professionals.

The assessment of whether the mention of a potentially upcoming medicine, before the time of the marketing authorization, is advertising (pre-launch), is difficult. A distinction must be drawn between advertising and information, including scientific mentioning, that is not advertising, which is especially difficult when the presentation of information must be assessed in a specific context with many nuances.

Advertising for medicinal products mean any form of door-to-door information, canvassing activity or inducement designed to promote the prescription, supply, sale or consumption of medicinal products referred to in section 1 (1), of the Executive Order on advertising, etc. for medicinal products.

Although the definition of advertising for medicines in the legislation is very broad, it does not mean that any mention of a pharmaceutical company's potentially upcoming medicines is advertising. This depends on what the purpose and content of the mention is, and whether the references e.g. is included in a professional/scientific framework that has a purpose other than to promote the prescription, supply, sale and consumption of the medicine.

1.1. Scientific mentioning or advertising?

The Investigator Panel assess whether an event should be regarded as scientific or as an advertising activity, in accordance with the decision by 28 May 2014 from the Danish Health Authority (now the Danish Medicines Agency), which is also mentioned in the Guidance to the Promotion Code. The case regarded whether a satellite symposium held at an international congress in Copenhagen should be regarded as a commercial activity or as an activity included in the scientific program of the congress, and that could be considered lawful information.

The Danish Health Authority noted that not all forms of mentioning of a medicinal product is advertising. "*This could be teaching, a professional presentation of scientific data and a professional review of studies, which are conducted on a scientific basis and in a scientific forum, e.g. an international congress, which does not have a purpose, that are covered by the definition of advertising of medicinal products, and thus are not advertising.*"

The Danish Health Authority states in their decision that it is the Authority's opinion, that "*the lecturers' presentations on the satellite symposia at the congress had a professional content, and that this was professional presentations of scientific data and studies given to healthcare professionals. The presentations are presented in a scientific forum.*" Further, the Danish Health Authority stated in their decision, that the Authority had noted that, "*the satellite symposia was part of the official scientific program for ECTRIMS in Copenhagen, and that it was the external lecturers who themselves had decided the design, content and the angle on the topic in the presentations.*" [ENLI's underline]

It should therefore be based on a specific assessment, whether it is advertising for medicines or compliant information.

A pharmaceutical company's mention of the results of the studies for a potential future medicine may be illegal advertising (pre-launch) for a non-approved medicine or legal information. It must be based on a specific assessment of the form, content and context in which the studies are referred to, when it is assessed whether there is a case of illegal advertising or lawful information. Whether pharmaceutical companies' mention of potential future medicines are considered illegal advertising (pre-launch) or information in the form of scientific reference will greatly depend on the context, that the studies regarding the potentially upcoming medicines is referred to, and of the form and content of the reference.

1.2. Indications on pre-launch/unlawful advertising

There are some clear indications of when the mention of scientific studies, as a main rule, is considered pre-launch/unlawful advertising:

1. The pharmaceutical company has published its phase III-studies,
2. The pharmaceutical company has submitted its application for marketing authorization to the relevant authorities,
3. The pharmaceutical company has a "positive opinion" from the EMA/FDA[1],
4. The pharmaceutical company knows the results from its phase III study and may also have a positive interim analysis, or
5. The pharmaceutical company is in the process of an indication expansion-study on an already approved medicine.

The following are comments on mention of respectively phase I, II and III studies, some illustrative scenarios as well as answers to some of the questions that has already been answered by ENLI.

1.2.1. Phase I and II studies

As a starting point ENLI considers mentioning of scientific reference of studies and data related to phase I and II of a development program for potential future medicines to HCP's, as information that falls outside the scope of the Promotion Code.

This is due to the fact that this concerns the exchange of information related to an early stage of development, and that it is not a given that the full development program results in a marketing authorization for a specific medicinal product. Such mentioning shall be deemed as scientific information, when information is presented in a neutral and non-promotional way. Mention of the potentially upcoming medicine should thus not be laudatory.

[1] If the drug is approved by the FDA, mention of this in Denmark is considered advertising in breach of the Promotion Code, Art.4, sec. 1 (advertising of a medicinal product that is not approved for marketing in the EU/Denmark)

1.2.2. Phase III studies

At the mention of information from phase III studies, one must particularly consider whether information exchange can be considered as advertising. Indicators for this could be that an application for marketing authorization is in preparation, or the publication of the results of the study are imminent. Mention of results from the phase III trial, after publication in a scientific journal[2], or by any other of the 5 above indications can be illegal advertising (pre-launch), for example when this reference contains claims of the medicine, and the company is working towards obtaining a marketing authorization. It must be based on a specific assessment of the form, content and context in which the results are referred to, when it is assessed whether there is a case of illegal advertising or lawful information.

It is thus particularly mention of phase III studies, which can pose a challenge in relation to whether the advertising rules and ENLI's Promotion Code must be complied with.

2. Illustrative scenarios regarding mention of studies in phase III

1. In commercial contexts, e.g. on exhibition stands in relation with scientific congresses, information on the phase 3 study regarding design and hypothesis can be provided, if the study is in the early part of phase III. It can be brief information with a focus on the study and the purpose of the study. It should be noted that the mentioning, which relate directly to the medicine (i.e. mention of trade and/or generic name) and statements regarding e.g. preliminary results, will not be regarded as scientific mentioning of studies and data, but as advertising.

2. At the presentation of pipelines in a commercial context, e.g. on an exhibition stand, information on the active substance, inter alia, the overall disease area, the more sub-specific disease area investigated, brief information on the medicine's mechanism and showing, what stage the clinical development of the medicinal product are in, can be provided. This information may also appear when mentioning a phase III study – if in the early part/an early stage, i.e. before the company has results from the study. One should stick to the molecule name and not mention the pharmaceutical name. It may, on the basis of a specific assessment of the mention of the study, be considered advertising if one uses the trade name, since it signals that one wants to advertise the upcoming medicine. Mention that relate directly to the medicine (i.e., with mention of trade and/or generic name), is considered, as a starting point, as advertising.

3. Mention of clinical development programs for an already approved medicine for the purpose of extension of indication, e.g. on an exhibition booth, will (usually) be considered illegal advertising of non-approved indications. As the medicinal product already has a marketing authorization, it may therefore only be referred to with the indication for which it is approved.

[2] I.e. after e-publishing with DOI number or print in a recognized journal with independent peer review, see. Promotion Code Art. 7

3. Q & A's

General

1. How to deal with studies, which examines the indication extensions of already approved medicines?

   ANSWER: Basically, a pharmaceutical company's mention of studies related to the indication extensions of the already authorized medicinal products, will be regarded as illegal advertising for a non-approved indication.

2. Are there recommendations for what kind of references you can use regarding information from phase I and phase II?

   ANSWER : If it's not advertising, there is no requirement for type of reference. If it is considered that it is advertising of a medicinal product, it will be illegal advertising (pre-launch).

3. How about competing medicines - what are the guidelines for mention here? If, for example a pipeline product combined with a market competitor. Can the competitor's generic name or brand name be mentioned? And may it be included in the pipeline overview?

   ANSWER: It is assumed that the company's purpose is not to advertise the competing product, so if you are not promoting the upcoming combination medicines, it may be lawful to mention. If one only informs on the study design, it is not considered advertising.

4. Is phase II equivalent to phase III, if a company submits an application for registration/"filing" based on phase II data?

   ANSWER: Yes. If you are submitting your application for registration after phase II, the illustrative scenarios, etc. for phase III, applies to phase II.

5. The medicine is not yet approved. Will the distribution of reprints of publications with phase II data be regarded as pre-launch/unlawful advertising? And how is it with phase III data?

   ANSWER: It depends on how far the development of the medicinal product is. If the medicinal product is at the end of phase III, and one thus know the results and is about to apply for approval of the medicine, or other of the above 5 indications for pre-launch, there may be a case of illegal advertising (pre-launch) by supplying reprints of publications from both phase II and III.

Pipelines

6. Is it allowed to disclose the generic name and/or indication in a pipeline overview for phase I and phase II and possibly ongoing phase III studies?

- Example:
  - Area: X
  - Compound: Z
  - Mechanism: Y
  - Area under investigation: W
  - Phase: Phase II, ongoing

ANSWER: One should stick to the molecule name, if the purpose of the reference is to inform, and not to advertise. Generic names should only appear in scientific contexts (congresses, meetings in medical societies, etc., where pharmaceutical companies do not organize or advertise).

7. Is it permissible to show ongoing studies in phase I and II at an exhibition e.g. with "Study XXXXX for metastatic breast cancer: title of study – phase II, now enrolling"? So one specifically shows which studies are currently in progress, and that these are active in relation to the inclusion of patients? And what about the ongoing phase III studies?

ANSWER: Mention (non-laudatory) of the phase I and II studies shall not be considered as advertising, and it is thus allowed to notify that, for example, one is including patients in a phase II study. With regard to an ongoing phase III study, one must look at how far one is in the study regarding whether information on the study is considered scientific mention or pre-launch of a potential future medicine. Moreover, reference is made to the illustrative scenarios regarding mention of phase III studies above.

8. Is it permissible to show even more for phase I and II – for example to show factual data as e.g. design, hypothesis, the number of patients, baseline characteristics of these patients, and results – e.g. XX1234 showed effect on ZZ with p-value of 0. xxxx? And what about the ongoing phase III?

ANSWER: Mention of data from phase I and II shall be considered, as a starting point, to be legitimate scientific information. With regard to the phase III trial, there should not be mention of the results of the study referred, cf. above. Mention of factual information about design and hypothesis for phase III trial is not, however, considered advertising.

9. How about biosimilars; can one inform, that a biosimilar is in pipeline for e.g. a marketed medicine?

ANSWER: The starting point is no. However, it depends on where you are in the pipeline, and what the purpose of the reference is. It must be based on a specific assessment of the form, content and the context in which the mention of Biosimilar medicinal products are included.

Meetings, etc. with healthcare professionals

10. A hospital ward has requested a presentation from our company on our phase III study, and what we expect the results will show. Are we outside the scope of the rules on advertising here, where we specifically were asked for a presentation?

ANSWER: Whether it is a case of illegal advertising or lawful information, depends on a specific assessment of the content of the query from the hospital, the professional setup of the event, the form and content of the presentation.

However, it is ENLI's immediate view that a single presentation is not in itself capable of constituting a scientific forum, like, e.g. international congresses, where a presentation is included in a comprehensive scientific program, cf. the general comments. In this case (where there is a request for general information) it would probably not just be kept to answering one very specific question from a healthcare professional, which, as a starting point, is outside the scope of rules on advertising.

11. To what extent can a pharmaceutical company – before approval of a medicine is available – arrange sales visits with doctors? (actual visit will be done after the expected approval)

ANSWER: Generally, it would be considered advertising for a specific medicine, if one, in the contact with healthcare professionals, mention specific medicinal products. To the extent one invite/arrange sales visit before a medicine is approved, and one informs healthcare professionals that the meeting concerns the upcoming medicine, this will be a case of illegal advertising (pre-launch). One can therefore only mention a specific medicinal product when there is a marketing authorization and when the price (if Rx medicine) is reported to medicinpris.dk, see Promotion Code Art. 4(1).

It is acceptable to book an "annual meeting", etc., but without informing that this includes "new information" or the like. On the other hand, it would not be in accordance with the rules to write "Launch meeting of new product for the treatment of [xx]" or similar wording.

12. When can the company invite to a launch symposium with an invitation, which refers to the new medicine?

ANSWER: See the answer to Q11.

13. Several pharmacies think we are arrogant because we only tell them about new medicines right up until they become available to pharmacies. Thus, they would like us to inform them in better time about future medicines. But can we?

ANSWER: It is considered advertising when informing pharmacies about upcoming medicines. This is partly because they are potential buyers of the medicines.

Therefore, you can only inform about the medicines when you have a marketing authorization, and for pharmacy-only (Rx) medicines, these must also be reported to the Danish Medicines Agency at least 14 days before. If a written request is received from an employee of the pharmacy before the above conditions are met, it will be a specific assessment of whether section 2 (2) (individual correspondence) of the Advertising Order is relevant, as answering such a request according to the circumstances may be seen as individual correspondence that serves to answer a specific question about a particular medicine.

14. Can an employee from the company show a presentation with phase III data, when the presentation is not branded, but kept in neutral colors and the medicine is only referred to by the generic name or research abbreviation (XX-123)? Does it make a difference, whether the employee is employed in the medical or the commercial department? Can the employee present phase II data, as described above?

ANSWER: Mention of data from studies in phase I and II shall be considered, as a starting point, to be legitimate scientific information. Mention of data from phase III can, however, after a specific assessment be considered illegal advertising (pre-launch). With regard to the phase III trial, this can e.g. be considered as illegal advertising (pre-launch), if the purpose is to inform on the positive results from the study. Mention of factual information about design and hypothesis for phase III trial is not, however, in itself advertising. One should stick to the molecule name and not mention the name of the medicinal product/generic name, since this could be considered advertising pending a specific assessment of the presentation.

It is irrelevant whether it is an employee who is employed in the medical or the commercial department of the company, who provides the presentation. ENLI is aware of, that companies can have internal guidelines regarding who can answer questions from healthcare professionals or provide information about specific medicines, but all of ENLI's codes (and Danish legislation in general) applies to all the employees of the company in their interactions with healthcare professionals. It is thus subordinate which department you are employed in, or what title you have - to the outside world you are the company's representative, and the company is subject to ENLI's rules and legislation, including the Advertising Order.

This means, among other things, that it makes no difference whether it is a medical adviser or a sales consultant who gives the presentation for a group of doctors, who e.g. requested knowledge about the company's future medicines. The rules on the prohibition of pre-launch and off-label reference applies to all the company's employees.

15. Can you have information on the company's medicine approved by the FDA in the United States at an exhibition stand at an international congress in Denmark? The medicine has not yet been approved in Denmark, but most of the participants at the congress are from abroad, so it is not predominantly Danish participants at the congress.

ANSWER: No. Danish law applies at a congress on Danish soil. One must not mention a medicine that does not have a valid marketing authorization in Denmark, cf. art. 4 (1) of the Promotion Code.

Consultancy services, including Advisory Boards

16. To what extent can the pharmaceutical company present data for medicinal products not yet approved, in an Advisory Board meeting?

ANSWER: Healthcare professionals who participate as professional consultants in an advisory board, can receive a presentation of data for a non-approved medicine, without it being perceived as advertising, if the presentation is necessary for a professional task which they must perform for the pharmaceutical company.

17. May the company in conjunction with an Advisory Board meeting hand out a copy of the PowerPoint presentation containing phase III data for a medicinal product not yet approved? The included data can be from either phase III publication or data that are not yet fully published (abstracts/posters or data on file)

ANSWER: Yes, if the material is necessary for the participants' performing of their tasks in an advisory board.

18. Speakers training: Will a doctor's participation in a European speaker training for a not yet authorized medicinal product be found to be pre-launch towards the concerned doctor? Does it make a difference whether the medicinal product is already approved with the concerned indication outside the EU, e.g. in the United States?

ANSWER: If there is an agreement with the concerned doctor, because he/she shall give a presentation on the upcoming medicine, it may be lawful to mention not yet approved medicines, when this is necessary for the task.

Market analyses

19. Will a market analysis be regarded as pre-launch, if the company (or a market research Institute, on behalf of the company) ask questions about a not yet authorized medicinal product; for example, by presenting phase III data for anonymized 'product X '? (Data is the actual data for an upcoming medicine, but are anonymized in the market survey)

ANSWER: It depends on a specific assessment of the questions whether the purpose of the presentation of phase III data is to advertise the medicine. If it is a market study, in which the company is anonymous, and the medicinal product cannot be identified, there will be no case of advertising.

20. Does it make a difference whether the market analysis as discussed in Q19, is performed by (or by a third party on behalf of) the company's European Office?

ANSWER: No

Press releases and inquiries from journalists

21. May we mention the approval of a new medicine by the US authorities in a Danish press release? The medicine has not yet been approved in Denmark, but we expect an approval in the near future.

ANSWER: Press releases will not be considered advertising, as a starting point, if:

- *It contains brief, objective information on a medicinal product*
- *It has general news value*
- *It has the press as target group and*
- *It is circulated or made available to a multiplicity of journalists or the media for the purpose of journalistic review and processing prior to publication.*

A pharmaceutical company can make a press release available to the media in the press-room of its website for about three weeks. After that, it will no longer be regarded as having general news value and may after a specific assessment be regarded as advertising.

Approval of a new medicine by foreign authorities may have general news value and, moreover, relevant to disclose - provided this is done according to the above criteria.

22. If a journalist asks us about a medicine that has not yet been approved for marketing in Denmark, can we as a pharmaceutical company make a statement to the journalist about this?

ANSWER: Yes, you can. You can speak to a journalist about matters relating to the company's future medicines on the Danish market. However, one must be careful not to praise the medicine, and thus advertising the medicine. In the conversation with a journalist, oral advertising may occur, in which case it will be an advertisement for an unapproved medicine, and possibly also a violation of the ban on advertising of a prescription medicine to the public (if the journalist is not a healthcare professional).