European evidence-based (S3) guideline for the treatment of acne – update 2016 – short version

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Conflict of interest
Please see Methods report of the European evidence-based (S3) guideline for the treatment of acne - update 2016 (DOI: 10.1111/jdv.13783).

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Corporate partners of the EDF have been asked to contribute towards this work. GlaxoSmithKline plc. (GSK) and Meda AB have contributed funding for the development of the European evidence-based (S3) guideline for the treatment of acne (update 2016) through an educational grant to the EDF. Sponsors had no influence on the content of the guideline. Support was given independent of any influence on methods or results. Sponsors did not receive any information about methods, group members or likely results. The sources of the funding were not known to the experts of the guideline and were not disclosed before the finalization of the guideline.

This is a short summary of the complete version of the S3 European Acne guideline, please see online appendix for full text (Document S1. Long Version) and detailed methods report (DOI: 10.1111/jdv.13783). Expiry date: 31 December 2020

Methods
In order to weight the different recommendations, the group assigned a ‘strength of recommendation’. It considered all aspects of the treatment decision, such as efficacy, safety, patient preference and the reliability of the existing body of evidence.

Strength of recommendation
In order to grade the recommendation a “standardized guideline” language was used:
1 is strongly recommended
2 can be recommended
3 can be considered
4 is not recommended
5 may not be used under any circumstances
6 a recommendation for or against treatment X cannot be made at the present time
Induction therapy

Summary of therapeutic recommendations for induction therapy

Recommendations are based on available evidence and expert consensus. Available evidence and expert voting lead to classification of strength of recommendation.

<table>
<thead>
<tr>
<th>Comedonal acne</th>
<th>Mild to moderate papulopustular acne</th>
<th>Severe papulopustular/moderate nodular acne</th>
<th>Severe nodular/conglobate acne</th>
</tr>
</thead>
<tbody>
<tr>
<td>High strength of recommendation</td>
<td>Adapalene + BPO (f.c.) or BPO + Clindamycin (f.c.)&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Isotretinoin</td>
<td>Isotretinoin</td>
</tr>
<tr>
<td>Medium strength of recommendation</td>
<td>Azelaic acid or BPO or Topical Retinoid&lt;sup&gt;4&lt;/sup&gt; or Topical Clindamycin + Tretinoin (f.c.)&lt;sup&gt;5,6&lt;/sup&gt; or Systemic Antibiotic&lt;sup&gt;5,7,8&lt;/sup&gt; + Adapalene&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + Adapalene&lt;sup&gt;9&lt;/sup&gt; or Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + Azelaic acid&lt;sup&gt;10&lt;/sup&gt; or Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + Isotretinoin + BPO (f.c.)</td>
<td>Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + Adapalene or Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + BPO (f.c.)</td>
</tr>
<tr>
<td>Low strength of recommendation</td>
<td>Azelaic acid or BPO</td>
<td>Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + BPO&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + Adapalene&lt;sup&gt;8,11&lt;/sup&gt; or Systemic Antibiotics&lt;sup&gt;5,8&lt;/sup&gt; + BPO&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alternatives for females&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-</td>
<td>Hormonal Anti-androgens + Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + Topicals (apart from antibiotics) or Hormonal Anti-androgens + Topical Treatment (apart from antibiotics)</td>
<td>Hormonal Anti-androgens + Systemic Antibiotic&lt;sup&gt;5,8&lt;/sup&gt; + Topicals (apart from antibiotics) or Hormonal Anti-androgens + Topical Treatment (apart from antibiotics)</td>
</tr>
</tbody>
</table>

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<sup>1</sup>Limitsations can apply that may necessitate the use of a treatment with a lower strength of recommendation as a first line therapy (e.g. financial resources/reimbursement limitations, legal restrictions, availability, drug licensing).

<sup>2</sup>Low strength of recommendation.

<sup>3</sup>The recommendation for comedonal treatment passed with vote of 60% agreement only, see chapter 5.1 in long version for more details.

<sup>4</sup>Adapalene to be preferred over tretinoin/isotretinoin (see chapter 5.4.1 in long version).

<sup>5</sup>Prescribers of antibiotics should be aware of the potential risk of the development of antibiotic resistances.

<sup>6</sup>The f.c. of clindamycin/tretinoin shows comparable efficacy and safety to the f.c. of BPO/clindamycin; downgrading to a medium strength of recommendation was done based on general concerns with respect to the development of antibiotic resistance.

<sup>7</sup>In case of more widespread disease/moderate severity, initiation of a systemic treatment can be recommended.

<sup>8</sup>Doxycycline and lymecycline (see chapter 5.4.2 in long version), limited to a treatment period of 3 months.

<sup>9</sup>Only studies found on systemic AB + adapalene; topical isotretinoin and tretinoin can be considered for combination treatment based on expert opinion.

<sup>10</sup>Indirect evidence from nodular and conglobate acne and expert opinion.

<sup>11</sup>Indirect evidence from severe papulopustular acne.

<sup>12</sup>Indirect evidence from a study also including chlorhexidin, recommendation additionally based on expert opinion.

<sup>13</sup>Systemic treatment with corticosteroids can be considered. t.c., fixed combination.

BPO, benzoyl peroxide.
Treatment of comedonal acne

Recommendations for comedonal acne

High strength of recommendation
None

Medium strength of recommendation
Topical retinoids can be recommended for the treatment of comedonal acne.

Low strength of recommendation
Azelaic acid can be considered for the treatment of comedonal acne.
BPO can be considered for the treatment of comedonal acne.

Open recommendation
A recommendation for or against treatment of comedonal acne with visible light as monotherapy, lasers with visible wavelengths and lasers with infrared wavelengths, with intense pulsed light (IPL) and photodynamic therapy (PDT) cannot be made at the present time.

Negative recommendation
Topical antibiotics are not recommended for the treatment of comedonal acne.
Hormonal anti-androgens, systemic antibiotics and/or systemic isotretinoin are not recommended for the treatment of comedonal acne.
Artificial ultraviolet (UV) radiation is not recommended for the treatment of comedonal acne.

1 Limitations can apply that may necessitate the use of a treatment with a lower strength of recommendation as a first line therapy (e.g. financial resources/reimbursement limitations, legal restrictions, availability, drug licensing).
2 Adapalene to be preferred over tretinoin/isotretinoin (see chapter 5.4.1 in long version).

Reasoning

General comment Only one trial looks specifically at patients with comedonal acne. As a source of indirect evidence, trials including patients with papulopustular acne were used and the percentage in the reduction of non-inflammatory lesions was considered as the relevant outcome parameter. Because of the general lack of direct evidence for the treatment of comedonal acne, the strength of recommendation was downgraded for all considered treatment options, starting with medium strength of recommendation as a maximum.

Due to the usually mild to moderate severity of comedonal acne, generally, a topical therapy is recommended.

The best efficacy was shown for topical retinoids, BPO and azelaic acid.

The tolerability of topical retinoids and BPO is comparable; there is a trend towards azelaic acid having a better safety/tolerability profile than BPO and a comparable profile to adapalene (indirect evidence, see Table 11 in long version).

The fixed-dose combination of adapalene with BPO shows a trend towards better efficacy against non-inflammatory lesions (NIL) when compared to BPO and a comparable efficacy when compared to adapalene (see Table 4 in long version). However, there is also a trend towards inferiority of the fixed combination with respect to the safety/tolerability profile (indirect evidence, see Table 12 in long version).

The fixed-dose combinations of clindamycin with BPO showed a trend towards better efficacy against non-inflammatory lesions (NIL) when compared to BPO and a comparable efficacy when compared to adapalene (see Table 4 in long version). With respect to the safety/tolerability profile, the combination is comparable to its single components (indirect evidence, see Table 12 in long version).

Few and only indirect data on patient preference are available. They indicate patient preference for adapalene over other topical retinoids.

Additional pathophysiological considerations favour the use of topical retinoids (reduction of microcomedones).
### Treatment of papulopustular acne

#### Recommendations for mild to moderate papulopustular acne

| **High strength of recommendation** | The fixed-dose combination adapalene and BPO is strongly recommended for the treatment of mild to moderate papulopustular acne. | The fixed-dose combination BPO and clindamycin is strongly recommended for the treatment of mild to moderate papulopustular acne. |
| **Medium strength of recommendation** | Azelaic acid can be recommended for the treatment of mild to moderate papulopustular acne. | BPO can be recommended for the treatment of mild to moderate papulopustular acne. | A combination of a systemic antibiotic with adapalene can be recommended for the treatment of moderate papulopustular acne. |
| **Low strength of recommendation** | Oral zinc can be considered for the treatment of mild to moderate papulopustular acne. | A combination of a systemic antibiotic with azelaic acid can be considered for the treatment of mild to moderate papulopustular acne. | The fixed-dose combination clindamycin and tretinoin can be recommended for the treatment of mild to moderate papulopustular acne. |
| **Open recommendation** | Due to a lack of sufficient evidence, a recommendation for or against treatment of mild to moderate papulopustular acne with red light, IPL, Laser or PDT cannot be made at the present time. | A combination of a systemic antibiotic with adapalene in fixed-dose combination with BPO can be considered for the treatment of moderate papulopustular acne. |
| **Negative recommendation** | Topical antibiotics as monotherapy are not recommended for the treatment of mild to moderate papulopustular acne. | The fixed-dose combination of erythromycin and isotretinoin can be considered for combination treatment based on expert opinion. | The fixed-dose combination of erythromycin and tretinoin can be considered for the treatment of mild to moderate papulopustular acne. |

1 Limitations can apply that may necessitate the use of a treatment with a lower strength of recommendation as a first line therapy (e.g. financial resources/reimbursement limit, legal restrictions, availability, drug licensing).

2 Prescribers of antibiotics should be aware of the potential risk of the development of antibiotic resistances.

3 Doxycycline and lymecycline (see chapter 5.4.2 in long version), limited to a treatment period of 3 months.

4 In case of more widespread disease/moderate severity, initiation of a systemic treatment can be recommended.

5 Only studies found on systemic AB + adapalene; isotretinoin and tretinoin can be considered for combination treatment based on expert opinion.

6 The f.c. of clindamycin/tretinoin shows comparable efficacy and safety to the f.c. of BPO/clindamycin; downgrading to a medium strength of recommendation was done based on general concerns with respect to the development of antibiotic resistance.

7 Adapalene to be preferred over tretinoin/isotretinoin (see chapter 5.4.1 in long version).

8 Indirect evidence from nodular and conglobate acne and expert opinion.

9 Indirect evidence from severe papulopustular acne.

10 Indirect evidence from a study also including chlorhexidin, recommendation additionally based on expert opinion.
Recommendations for severe papulopustular/moderate nodular acne

<table>
<thead>
<tr>
<th>High strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral isotretinoin monotherapy is strongly recommended for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Medium strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic antibiotics in combination with adapalene, with the fixed-dose combination of adapalene and BPO, or in combination with azelaic acid can be recommended for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic antibiotics in combination with BPO can be considered for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
<tr>
<td>For females: Hormonal anti-androgens in combination with systemic antibiotic and topicals (apart from antibiotics) can be considered for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
<tr>
<td>For females: Hormonal anti-androgens in combination with a topical treatment (apart from antibiotics) can be considered for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Open recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Due to a lack of sufficient evidence, a recommendation for or against treatment of severe papulopustular/moderate nodular acne with red light, IPL, laser or PDT cannot be made at the present time.</td>
</tr>
<tr>
<td>Although PDT is effective in the treatment of severe papulopustular/moderate nodular acne, a recommendation for or against its use cannot be made at the present time due to a lack of standard treatment regimens that ensure a favourable profile of acute adverse reaction.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Negative recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single or combined topical monotherapy is not recommended for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
<tr>
<td>Oral antibiotics as monotherapy are not recommended for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
<tr>
<td>Oral anti-androgens as monotherapy are not recommended for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
<tr>
<td>Visible light as monotherapy is not recommended for the treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
<tr>
<td>Artificial UV radiation sources are not recommended as a treatment of severe papulopustular/moderate nodular acne.</td>
</tr>
</tbody>
</table>

Reasoning

Monotherapy with azelaic acid, BPO or topical retinoids showed superior efficacy when compared with vehicle.

Adapalene, azelaic acid and BPO showed comparable efficacy when compared with each other. When comparing the topical retinoids (adapalene, isotretinoin and tretinoin) directly against each other, no relevant difference with respect to efficacy was seen. Some conflicting evidence to the comparability of the efficacy of the treatment options above arises, when looking at the other head to head comparisons indicating superiority of BPO over isotretinoin and tretinoin over azelaic acid.

With respect to the fixed combinations, BPO/clindamycin shows superiority over both single components.

The three fixed combinations of adapalene/BPO, clindamycin/tretinoin as well as erythromycin/isotretinoin show superiority to one of the components but not to both of the components when compared individually.

Head to head comparisons of the fixed combinations of adapalene/BPO vs. BPO/clindamycin as well as head to head comparisons of clindamycin/tretinoin vs. BPO/clindamycin show comparable efficacy.

Due to the serious concerns regarding the risk of developing antibiotic resistance, topical monotherapy with antibiotics is generally not recommended. The potential risk of developing antibiotic resistance was taken into consideration by the expert group. It led to a medium strength of recommendation for the fixed combination of clindamycin/tretinoin despite comparable efficacy and safety when compared to the fixed combination of BPO/clindamycin. The differentiation between clindamycin/tretinoin (medium strength of recommendation) and erythromycin/isotretinoin (low strength of recommendation) was based on evidence showing the lack of development of antibiotic resistance after 16 weeks of treatment with clindamycin/tretinoin as well as indirect evidence on stronger development of antibiotic resistance to erythromycin and expert opinion on better follicular penetration and galenic of the clindamycin/tretinoin f.c. formulation.

Monotherapy with azelaic acid, BPO or topical retinoids showed comparable efficacy when compared with each other.

For severe cases, systemic treatment with isotretinoin is recommended based on the very good efficacy seen in clinical practice.

The available evidence on safety and tolerability is extremely scarce and was considered insufficient to be used as a primary basis to formulate treatment recommendations.

The lack of standardized protocols, experience and clinical trial data mean there is insufficient evidence to recommend the
treatment of papulopustular acne with laser and light sources other than blue light.

Choice of topical vs. systemic treatment
There are limited data comparing topical treatments with a systemic treatment or the additional effect of a combination of a topical plus systemic vs. topical treatment only. Most of the available trials compare a topical antibiotic monotherapy with a systemic antibiotic monotherapy.

Treatment of severe nodular/conglobate acne

Recommendations for severe nodular/conglobate acne

<table>
<thead>
<tr>
<th>High strength of recommendation</th>
<th>Oral isotretinoin is strongly recommended as a monotherapy for the treatment of severe nodular/conglobate acne.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium strength of recommendation</td>
<td>Systemic antibiotics (^2,3) in combination with the fixed-dose combination of adapalene and BPO or in combination with azelaic acid can be recommended for the treatment of severe nodular/conglobate acne.</td>
</tr>
<tr>
<td>Low strength of recommendation</td>
<td>Systemic antibiotics (^2,3) in combination with adapalene (^4,5) or BPO (^5) can be considered for the treatment of severe nodular/conglobate acne. For females: Hormonal anti-androgens in combination with systemic antibiotic (^2,3) and topicals (apart from antibiotics) can be considered for the treatment of severe nodular/conglobate acne. For females: Hormonal anti-androgens in combination with a topical treatment can be considered for the treatment of severe nodular/conglobate acne.</td>
</tr>
<tr>
<td>Open recommendation</td>
<td>Due to a lack of sufficient evidence, it is currently not possible to make a recommendation for or against treatment with IPL or laser in severe nodular/conglobate acne. Although PDT is effective in the treatment of severe nodular/conglobate acne, it cannot yet be recommended due to a lack of standard treatment regimens that ensure a favourable profile of acute adverse reaction.</td>
</tr>
<tr>
<td>Negative recommendation</td>
<td>Topical monotherapy is not recommended for the treatment of conglobate acne. Oral antibiotics are not recommended as monotherapy for the treatment of severe nodular/conglobate acne. Oral anti-androgens are not recommended as monotherapy for the treatment of severe nodular/conglobate acne. Artificial UV radiation sources are not recommended for the treatment of severe nodular/conglobate acne. Visible light as monotherapy is not recommended for the treatment of severe nodular/conglobate acne.</td>
</tr>
</tbody>
</table>

1Limitations can apply that may necessitate the use of a treatment with a lower strength of recommendation as a first line therapy (e.g. financial resources/reimbursement limit, legal restrictions, availability, drug licensing).
2Prescribers of antibiotics should be aware of the potential risk of the development of antibiotic resistances.
3Doxycycline and lymecycline (see chapter 5.4.2 in long version), limited to a treatment period of 3 months.
4Only studies found on systemic AB + adapalene; isotretinoin and tretinoin can be considered for combination treatment based on expert opinion.
5Indirect evidence from severe papulopustular acne.

Reasoning

General comment Very few of the included trials (see long version) looked specifically at patients with nodular or conglobate acne. As a source of indirect evidence, studies of patients with severe papulopustular acne were used and the percentage in the reduction of nodules (NO) and cysts (CY) in these studies was used. In case of use of such indirect evidence, the strength of recommendation was downgraded for the considered treatment options. Systemic isotretinoin shows superior efficacy in the treatment of severe nodular/conglobate acne when compared with systemic antibiotics or topical therapy only.

The expert group considered that the greatest effectiveness in the treatment of severe nodular/conglobate acne in clinical practice is seen with systemic isotretinoin. This can only be partly supported by published evidence, due to the scarcity of clinical trials in conglobate acne. In the experts’ opinion, safety concerns with isotretinoin are manageable if treatment is properly initiated and monitored. Patient benefit with respect to treatment effect, improvement in quality of life and avoidance of scarring outweigh the side-effects.
General considerations

Choice of type of topical retinoid

Adapalene should be selected in preference to tretinoin and isotretinoin.

Choice of type of systemic antibiotic

Doxycycline and lymecycline should be selected in preference to minocycline and tetracycline.

Considerations on isotretinoin and dosage

For severe papulopustular acne/moderate nodular acne, a dosage of systemic isotretinoin of 0.3–0.5 mg/kg can be recommended.
For conglobate acne a dosage of systemic isotretinoin of ≥0.5 mg/kg can be recommended.
The duration of the therapy should be at least 6 months.
In case of insufficient response, the treatment period can be prolonged.

Maintenance therapy

Summary of therapeutic recommendations for maintenance therapy with respect to acne type before induction therapy

Recommendations are based on available evidence and expert consensus. Available evidence and expert voting lead to classification of strength of recommendation.

A maintenance treatment, especially for the patients with “particular need for a maintenance treatment” as defined below, is recommended. The low strength of recommendation provided below reflects primarily the lack of good evidence as to which is the best treatment and does not put into question the need for maintenance therapy in general.

<table>
<thead>
<tr>
<th>Comedonal acne</th>
<th>Mild to moderate papulopustular acne</th>
<th>Severe papulopustular/moderate nodular acne</th>
<th>Severe nodular/conglobate acne</th>
</tr>
</thead>
<tbody>
<tr>
<td>High strength of recommendation</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Medium strength of recommendation</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Low strength of recommendation</td>
<td>Azelaic Acid or Topical Retinoid ²</td>
<td>Azelaic Acid or BPO or Topical Retinoid ²</td>
<td>Adapalene + BPO (f.c.) ³</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>or Azelaic Acid or BPO ³</td>
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<tr>
<td></td>
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<td></td>
<td>or Low Dose Systemic Isotretinoin (max: 0.3 mg/kg/day)</td>
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<td></td>
<td></td>
<td></td>
<td>or Topical Retinoid ²</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Continued Hormonal Anti-androgens ⁴ + Topical Treatment (apart from antibiotics)</td>
</tr>
<tr>
<td>Alternatives for females ¹</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

¹Low strength of recommendation.
²Preference for adapalene over isotretinoin/tretinoin.
³In case of continuing inflammatory lesions.
⁴Refer to national guidelines and EMA recommendations for precautions with respect to risk and duration of hormonal anti-androgens/combined oral contraceptives.
### Recommendations for maintenance therapy

<table>
<thead>
<tr>
<th>High strength of recommendation</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium strength of recommendation</td>
<td>None</td>
</tr>
<tr>
<td>Low strength of recommendation</td>
<td>None</td>
</tr>
</tbody>
</table>

#### Comedonal acne
- Azelaic acid can be considered for the maintenance treatment of comedonal acne.
- Topical retinoid<sup>1</sup> can be considered for the maintenance treatment of comedonal acne.

#### Mild to moderate papulopustular acne
- Azelaic acid can be considered for the maintenance treatment of mild to moderate papulopustular acne.
- Topical retinoid<sup>1</sup> can be considered for the maintenance treatment of mild to moderate papulopustular acne.

#### Severe papulopustular/moderate nodular acne and severe nodular/conglobate acne
- The fixed-dose combination adapalene and BPO<sup>2</sup> can be considered for the maintenance treatment of severe papulopustular/moderate nodular acne and severe nodular/conglobate acne.
- Azelaic acid can be considered for the maintenance treatment of severe papulopustular/moderate nodular acne and severe nodular/conglobate acne.
- BPO<sup>2</sup> can be considered for the maintenance treatment of severe papulopustular/moderate nodular acne and severe nodular/conglobate acne.
- Low dose systemic isotretinoin (max. 0.3 mg/kg/day) can be considered for the maintenance treatment of severe papulopustular/moderate nodular acne and severe nodular/conglobate acne.
- Topical retinoid<sup>1</sup> can be considered for the maintenance treatment of severe papulopustular/moderate nodular acne and severe nodular/conglobate acne.
- For females: Continued hormonal anti-androgens<sup>3</sup> and topical treatment (apart from antibiotics) can be considered for the maintenance treatment of severe papulopustular/moderate nodular acne and severe nodular/conglobate acne.

#### Open recommendation
- Due to a lack of sufficient evidence, it is currently not possible to make a recommendation for or against maintenance treatment with red light, blue light, IPL, laser, PDT or oral zinc.

#### Negative recommendation
- Topical and/or systemic antibiotics as monotherapy or combination therapy are not recommended for maintenance treatment of acne.
- Artificial UV radiation is not recommended for maintenance treatment of acne.

<sup>1</sup>Preference for adapalene over isotretinoin/tretinoin.
<sup>2</sup>In case of continuing inflammatory lesions.
<sup>3</sup>Refer to national guidelines and EMA recommendations for precautions with respect to risk and duration of hormonal anti-androgens/combined oral contraceptives.

### Reasoning
Available evidence indicates efficacy of azelaic acid, topical retinoids and adapalene/BPO over vehicle during maintenance treatment.

Pathophysiological data supports use of azelaic acid, topical retinoids and adapalene based on their demonstrated efficacy on microcomedones.

Any use of topical or systemic antibiotics is not recommended on a long-term base/during maintenance therapy.

### Disclaimer
The development of guidelines is a time and resource intensive process and currently no public funding is available for European guidelines. In order to be able to produce high quality guidelines, the EDF uses its membership contributions and asks its cooperative partners for support (see Funding source).

### Supporting information
Additional Supporting Information may be found in the online version of this article:
- Table S1. Comedonal acne.
- Table S2. Papulopustular acne.
- Table S3. Conglobate acne.
- Document S1. Long version.
- Document S2. Evaluated studies.
- Document S3. List of abbreviations.