

## Member's Evidence Request response

**Request Reference: ED20/151**

**Received: 25/05/2020**

**Completed: 09/06/2020**

### A: Question

Regarding self administration at home of sayana press for someone who was starting an injectable for the first time - how safe is this (in relation to anaphylaxis) to be done at home for women who have not already had DMPA or sayana (bearing in mind anaphylaxis can sometimes only manifest itself after the second injection)?

### B: Response

Anaphylaxis is an acute, systemic, potentially life-threatening immediate hypersensitivity reaction, involving the release of mediators from mast cells, basophils and recruited inflammatory cells. Anaphylaxis is defined by a number of signs and symptoms, alone or in combination, which occur within minutes, or up to a few hours, after exposure to a provoking agent. Most cases are mild but any anaphylaxis has the potential to become life-threatening. Severe initial symptoms develop rapidly, usually reaching peak severity within 3-30 minutes. Observation for at least 1 hour is required to ensure that a mild reaction is not progressing.[1,2]

Anaphylaxis may occur as a result of immunologic mechanisms (either IgE-dependent or IgE-independent), or non-immunologic mechanisms. Immediate onset hypersensitivity including anaphylaxis has been reported for a wide range of drugs. [1] The mechanism underlying anaphylactic reaction to DMPA injection (whether to MPA itself or an excipient) is not evident from the published literature.

The Summary of Product Characteristics (SPC) for Sayana<sup>®</sup> Press lists risk of anaphylactic response as 'not known' (cannot be estimated from the available data).[3] It notes "As this product contains methylparahydroxybenzoate [E218] and propylparahydroxybenzoate [E216], it may cause allergic reactions (possibly delayed), and exceptionally, bronchospasm." The SPC for Depo-Provera<sup>®</sup> states "Reports of anaphylactic responses (anaphylactic reactions, anaphylactic shock, anaphylactoid reactions) have been received" and lists anaphylactic reaction as a "rare" adverse reaction ( $\geq 1/10,000$  to  $< 1/1000$ ).[4] Depo-Provera also contains methylparaben (E218) and propylparaben (E216) - they are present in cosmetics and medicines to which individuals could have had prior exposure and be sensitised if IgE-mediated reaction was the mechanism of reaction..

The FSRH CEU identified no further data to further inform the risk of anaphylaxis associated with administration of Sayana Press or Depo Provera. As of 01/06/2020 (all reports processed from inception up to 30 April 2020), the Interactive Drug Analysis Profiles (iDAP) on Medicines and Healthcare products Regulatory Agency (MHRA) Yellow Card scheme website lists 94 reports of “anaphylactic reaction”, 13 of “anaphylactic shock” and 10 of “anaphylactoid reaction” for all medroxyprogesterone acetate (MPA)-containing drugs.[5] Listing of an adverse event in a DAP does not, however, confirm that the active drug or any of the product excipients caused the effect.

FSRH CEU literature review identified four published cases of anaphylaxis following IM depot medroxyprogesterone acetate (DMPA) injection. A 16-year-old girl had an anaphylactic reaction shortly after administration, having previously received four doses of DMPA with no reaction.[6] A 40-year-old woman with no previous apparent exposure to exogenous progestogen suffered an immediate anaphylactic reaction to a DMPA injection given at the time of surgical abortion; she had a similar response to repeat injection 12 weeks later.[7] Two older cases from 1993 and 1974 are also reported. [8,9] No published cases of anaphylactic reaction following administration of Sayana Press are identified.

### **Conclusion:**

Reported cases suggest that anaphylactic reaction has occurred with both first and subsequent exposures to IM DMPA. The provoking agent and mechanism for the response is not apparent. It is assumed that anaphylactic response could also be possible with both first and subsequent exposures to Sayana Press. In line with advice in the SPC for Sayana Press [3], individuals with known sensitivity to any excipient should not use the product. Self-administration of Sayana Press should be taught by a healthcare practitioner, but it is accepted practice that the product can be self-administered by the individual at home. The risk of anaphylactic reaction appears to be very low, however the FSRH CEU suggests that users can be advised to ensure that there is a competent adult present at the time of administration who is aware that they should call for emergency help at the time of onset of any relevant symptoms (see “Symptoms and Signs of Anaphylaxis” below).

### **Symptoms and Signs of Anaphylaxis[1,2]**

The initial manifestation of anaphylaxis may be loss of consciousness. Patients often describe "a sense of doom." In this instance, the symptoms and signs of anaphylaxis are isolated to one organ system, but since anaphylaxis is a systemic event, in the vast majority of subjects two or more systems are involved.

- *Gastro-intestinal:* Abdominal pain, hyperperistalsis with faecal urgency or incontinence, nausea, vomiting, diarrhea.
- *Oral:* Pruritus of lips, tongue and palate, edema of lips and tongue.
- *Respiratory:* Upper airway obstruction from angioedema of the tongue, oropharynx or larynx; bronchospasm, chest tightness, cough, wheezing; rhinitis, sneezing, congestion, rhinorrhea.
- *Cutaneous:* Diffuse erythema, flushing, urticaria, pruritus, angioedema.
- *Cardiovascular:* Faintness, hypotension, arrhythmias, hypovolemic shock, syncope, chest pain.
- *Ocular:* Periorbital edema, erythema, conjunctival erythema, tearing.
- *Genito-urinary:* Uterine cramps, urinary urgency or incontinence.

### C: Evidence-Based Medicine Question (which guided our literature search strategy)

<b>Population:</b>	<i>Women of reproductive age</i>
<b>Intervention:</b>	<i>Progestogen-only injectables</i>
<b>Outcome:</b>	<i>Anaphylactic reaction</i>

### D. References

1. Stone SF, Phillips EJ, Wiese MD, Heddle RJ, Brown SG. Immediate-type hypersensitivity drug reactions. *British journal of clinical pharmacology*. 2014 Jul;78(1):1-3.
2. World allergy Organization. Anaphylaxis: Synopsis. Updated September 2012. Available online [here](#) (accessed 09/06/2020)
3. Pfizer Limited. eMC. *Summary of Product Characteristics: SayanaPress 104mg/ 0.65 ml suspension for injection*. Last updated on emc on 16 May 2019. Available online [here](#) (accessed 09/06/2020)
4. Pfizer Limited. eMC. *Summary of Product Characteristics: Depo-Provera 150mg/ml Injection*. Last updated on emc 11 February 2020. Available online [here](#) (accessed 09/06/2020)
5. Medicines and Healthcare products Regulatory Agency. Yellow Card. Interactive Drug Analysis Profiles (iDAPs). Medroxyprogesterone. Available online [here](#) (accessed 01/06/2020)
6. Lestishock L, Pariseau C, Rooholamini S, *et al*. Anaphylaxis from depot medroxyprogesterone acetate in an adolescent girl. *Obstet Gynecol*. 2011 Aug;**118**(2 Pt 2):443-5.
7. Selo-Ojeme DO, Tillisi A, Welch CC. Anaphylaxis from medroxyprogesterone acetate. *Obstet Gynecol*. 2004 May;**103**(5 Pt 2):1045-6.
8. Brooks G. Anaphylactoid shock with medroxyprogesterone acetate: a case report. *J La State Med Soc* 1974;126: 397–9.
9. Rajapaksa DS. Anaphylaxis to Depo-Provera? *Ceylon Med J* 1993;38:158–69.

Checked by SMRH

Enquiry response by ZEC

The Clinical Effectiveness Unit (CEU) is funded by the FSRH and supported by NHS Lothian. The advice given in this Member's Enquiry Response has been prepared by the CEU and is based on a structured search and review of published evidence available at the date of preparation. The advice given here should be considered as guidance only. Adherence to it will not ensure a successful outcome in every case and it may not include all acceptable methods of care aimed at the same results. This response has been prepared as a service to FSRH members, but is not an official Faculty guidance product; Faculty guidance is produced by a different and lengthier process. It is not intended to be construed or to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances. Members are welcome to reproduce this response by photocopying or other means, in order to share the information with colleagues.