Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

DRUG ALERT

CLASS 2 MEDICINES RECALL

Action within 48 hours
Patient, Pharmacy and Wholesaler Level Recall

Date: 07 April 2020 EL (20)A/20 Our Ref: MDR 057-08/19

Dear Healthcare Professional,

Pharmaswiss Česka republika s.r.o. (an affiliate of Bausch & Lomb UK Limited)

Emerade 300 micrograms solution for injection in pre-filled syringe PL 33616/0014

(Adrenaline)

Brief description of the problem

Pharmaswiss Česka republika s.r.o. (an affiliate of Bausch & Lomb UK Limited) is recalling all unexpired batches of Emerade 300 microgram auto-injectors (also referred to as pens) from patients due to an error in one component of the auto-injector believed to cause some pens to fail to activate and deliver adrenaline.

This is a recall for Emerade 300 microgram pens only. This is a different alert to that issued on 04 March 2020 for Emerade 150 microgram auto-injectors.

Results from manufacturer testing of Emerade auto-injectors recalled from patients in Europe indicate that approximately 13% of pens need higher than normal force to activate, implying a higher risk of activation failure than was previously understood. This applies to all strengths of Emerade. Previous estimations of activation failure were obtained from tests on pens that had been stored in the manufacturing facility. Whereas, the recent results were obtained on pens carried by patients, suggesting an environmental contribution to the risk. Investigations are ongoing to understand this.

For Emerade 300 micrograms auto-injectors, the MHRA, in conjunction with the Department of Health & Social Care (DHSC) has established that there are sufficient supplies of alternative auto-injectors to allow a recall to patient level.

Healthcare professionals should inform patients and carers that they should therefore return all in-date Emerade 300 micrograms auto-injectors to their local pharmacy once they have obtained a prescription for, and been supplied with, an alternative brand.

The recall of Emerade 300 microgram auto-injectors from patients follows a previous recall of Emerade 150 microgram auto-injectors from patients. More information on the previous alert can be found in the link here.

At the point of prescribing and dispensing, it is vital that patients and carers receive training to ensure they are completely familiar with the use of the new device. This is because each brand of adrenaline auto-injector is used differently. **Patients should continue to carry two devices at all times**

in case of a need to administer a second dose of adrenaline before the arrival of the emergency services (see links to training material below).

General Practitioners (GPs) should send the attached letter "Advice for patients with an Emerade 300 microgram auto-injector" on page 7, to all patients and carers, as appropriate, who have been prescribed Emerade 300 micrograms auto-injectors.

Emerade 500 microgram auto-injectors are not being recalled. Unless previously actioned during the Emerade 150 microgram recall, GPs should send the attached letter "Advice for patients with Emerade 500 microgram auto-injectors" on page 8 and 9, to those patients who have been prescribed Emerade 500 microgram auto-injectors, for information. This information is available as separate PDFs in the link for this alert.

Actions for healthcare professionals

All healthcare professionals in primary, secondary or specialist healthcare services who prescribe, supply or administer adrenaline auto-injectors, or who advise patients and their carers, should ensure that they:

- identify patients who have been supplied with Emerade 300 micrograms auto-injectors and ensure they are reviewed to determine whether their adrenaline auto-injector prescription is still appropriate and in line with existing guidance;

- immediately inform patients and carers to request a new prescription to replace each Emerade 300 microgram auto-injector with one new adrenaline pen in an alternative brand. Healthcare professionals should be aware that the licensed dosing recommendations for each brand of pen are not identical. They are available in the Summary of Product Characteristics (SmPC) and should be followed (see links on page 3 below);

- inform patients to return Emerade 300 microgram auto-injectors to the pharmacy, when they have obtained two adrenaline auto-injectors in a different brand;
    - Although pens should be returned to a pharmacy once a replacement is obtained, this should not require someone who is self-isolating to leave their home (see COVID-19 advice on page 3)
    - **Pharmacists and pharmacies who receive Emerade 300 microgram auto-injectors from patients should quarantine the pens and return them to the supplier using the supplier's approved process.**

- inform patients:
    - that they should always carry two in-date auto-injectors with them at all times in case they need to administer a second dose of adrenaline before the arrival of the emergency services;
    - that they need to receive training, so they are confident in being able to use any new devices (see further information on page 3 below);
    - of the signs of anaphylaxis and the actions they should immediately take (see Management of Anaphylaxis on page 4 for further advice).

- are aware that this recall also applies to Emerade 300 microgram auto-injectors that are in emergency anaphylaxis kits held by healthcare professionals, such as dental surgery kits etc.

  - adrenaline ampoules, as opposed to auto-injectors, should be stocked when renewing the adrenaline in anaphylaxis kits (ensuring dosing charts, needles and syringes are included). See further information on page 4 below.
- are aware that this recall also applies to Emerade 300 microgram auto-injectors that are currently held by schools. See further information on the use of pens in school, page 5;

Prescribers should issue no more than two adrenaline auto-injectors per patient (of any brand or strength) unless:

- schools require separate pens to be kept on the school premises (e.g. in a medical room) in which case prescribers may need to consider issuing more than two but no more than four pens per child (of any brand or strength). See further information on the use of pens in school, page 4;

- for the rare scenario where patients might need more than two adrenaline pens prescribed (for example, a prior severe reaction resistant to treatment with adrenaline), where the prescriber may issue additional pens.

General Practitioners (GPs) should send the attached letter "Advice for patients who have been prescribed an Emerade 300 microgram auto-injector" on page 7, to all patients and carers, as appropriate, who have been prescribed Emerade 300 micrograms auto-injectors.

Information in relation to Coronavirus (COVID-19):

- When a prescription is needed for replacement pens, where possible, telephone appointments should be considered, based on the current UK Government guidelines for social distancing in relation to Coronavirus (COVID-19). Patients should be informed to follow the advice of their local GP practice/hospital and only attend where they are instructed to do so. Further information can be obtained on the government website: https://www.gov.uk/government/topical-events/coronavirus-covid-19-uk-government-response

- Healthcare professionals involved in the dispensing process may wish to consider how to ensure that vulnerable patients and those practising self-isolation, social distancing and shielding can still obtain their replacement auto-injectors, considering the use of delivery services where appropriate. Although pens should be returned to a pharmacy once a replacement is obtained, this should not require someone who is self-isolating or shielding to leave their home.

- At the present time, patients and carers may be unable to visit a healthcare professional to receive training in use of the new device. They must take particular care therefore to ensure that they read the instructions on how to use the pen in the leaflet contained in the box. Patients and carers should also consult training information for their new pen on the manufacturer's website This includes training videos. All the manufacturers also provide trainer pens on request (mock pens that do not contain a needle or adrenaline) for patients and carers to practise with. Patients are strongly urged to obtain these.

Patients and carers should be told of the important differences between brands of adrenaline pen in how they are used.

- Healthcare professionals – doctors, nurses and pharmacists – should, where possible, ensure they provide training to patients and carers in correct use of the new pen. Instructions for use can be found in the SmPC (prescriber's information) and in the Patient Information Leaflets (PILs) that are supplied with the different pens and on the respective manufacturers' websites where training videos are available. Training pens that do not contain adrenaline can also be obtained free of

charge from the manufacturers. Healthcare professionals and patients are strongly recommended to obtain these to assist with training. The trainer pens can be used repeatedly, allowing patients to practise regularly with them so they are prepared for use in an emergency.

- The following links provide training materials for the different devices:

  EpiPen
  - EpiPen® devices: http://www.epipen.co.uk/patients/epipenr-user-guide
  - EpiPen® 0.15mg: https://www.medicines.org.uk/emc/product/4290/rmms
  - EpiPen® 0.3mg: https://www.medicines.org.uk/emc/product/4289/rmms

  Jext
  - Jext® devices: https://jext.co.uk/
  - Jext® 150 Training Video: https://www.medicines.org.uk/emc/product/5747/rmms
  - Jext® 300 Training Video: https://www.medicines.org.uk/emc/product/5748/rmms

  Emerade
  - Emerade® devices: https://www.emerade-bausch.co.uk/patient/how-to-use-emerade
  - Emerade® 150: https://www.medicines.org.uk/emc/product/5278/rmms
  - Emerade® 300: https://www.medicines.org.uk/emc/product/5280/rmms
  - Emerade® 500: https://www.medicines.org.uk/emc/product/5279/rmms

Emergency Use Adrenaline Auto-injectors in the Healthcare setting: Adrenaline pens that are currently held by healthcare professionals, i.e. in emergency anaphylaxis kits, dental kits etc. are subject to the recall.

- Advice from DHSC is that healthcare professionals providing services where anaphylaxis treatment may be required should be competent to administer intramuscular adrenaline from ampoules with a syringe and needle. These services should use adrenaline from ampoules in preference to adrenaline auto-injectors. This is to preserve supplies of adrenaline pens for patients to self-administer, during the ongoing global fragile supply situation for all adrenaline auto-injectors.
- **Therefore, when re-stocking adrenaline in anaphylaxis kits all staff are alerted to stock these with ampoules (together with dosing charts for use of intramuscular adrenaline to treat anaphylaxis, needles and syringes) and not adrenaline pens (of any brand).**
- The Green Book and Resuscitation Council guidance provides additional advice to healthcare professionals on the use of adrenaline in response to anaphylaxis.

Management of anaphylaxis

All patients should be made aware of the signs and symptoms of anaphylaxis and that at the first onset of any signs or symptoms of anaphylaxis, they or a carer/bystander should:

- administer an adrenaline auto-injector device without delay, even if there is doubt whether it is anaphylaxis;
- call an ambulance (999) immediately after giving the injection and say this is an emergency case of anaphylaxis;
- administer a second auto-injector 5 to 15 minutes after the initial dose, if no improvement is seen or if the patient deteriorates after an initial improvement;
- for patients who hold in-date Emerade 500 mcg pens that are not being recalled, patients should be advised to use a second adrenaline auto-injector immediately if an Emerade pen fails to activate despite pressing firmly against the thigh (pictorial guidance on whether an Emerade pen has activated or not is given at the end of this alert on page 10);

- make further attempts to activate a failed Emerade pen while waiting for the ambulance if the patient is not improving, even if one pen has worked, as this may suggest a need for a second or more doses. The purpose of adrenaline pens is to start treatment for anaphylaxis that is continued by the emergency services.

Guidance on the use of adrenaline auto-injectors in schools:
For more information on the use of adrenaline auto-injectors in schools, see the link below:
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/645476/Adrenaline_auto_injectors_in_schools.pdf

- Children at risk of anaphylaxis should have their prescribed adrenaline auto-injectors at school for use in an emergency.
- Depending on their level of understanding and competence, children and particularly teenagers should carry their adrenaline pens with them at all times or the pens should be quickly and easily accessible at all times. If the adrenaline auto-injectors are not carried by the pupil, then they should be kept in a central place in a box marked clearly with the pupil's name but NOT locked in a cupboard or an office where access is restricted.

Information on Emerade 500 microgram auto-injectors

- **Unless previously shared, patients with Emerade 500 microgram auto-injectors should be provided with the supplementary letter and information available on pages 8/9 and the information from page 10 and 11. The letters for patients can be found as additional links on the page where this alert is issued.**

Emerade 500 microgram auto-injectors are not being recalled at present as there are insufficient supplies of alternatives to provide replacements. For all patients currently in possession of Emerade 500 microgram auto-injectors, the advice from MHRA and DHSC remains that the risk to the patient of being left without a pen, and therefore having no adrenaline to administer, is greater than allowing them to keep pens that may not activate, especially if two pens are carried. Although the risk of activation failure is now estimated to be higher than was previously reported, most Emerade pens will still activate as intended. Therefore, patients should be advised to retain their unexpired Emerade 500 microgram pens, to avoid being left without access to any adrenaline pens. Further MHRA drug alerts will be issued with immediate effect, as soon as supplies of alternatives are able to meet the demand for replacement of all the remaining Emerade pens held by patients.

Patients and carers should be informed that they must follow existing advice to carry two pens with them at all times and for the patient/bystander to dial 999 immediately after administration of an adrenaline pen. The purpose of adrenaline pens is to start treatment for anaphylaxis, which is then continued by the emergency services.

Patients whose Emerade 500 microgram pens are due to expire will need to replace them with pens of an alternative brand. Pharmacies and wholesalers in the UK are no longer stocking Emerade. Prescribers and patients can be reassured that the alternative brands in the UK – EpiPen and Jext, available in a maximum strength of 300 micrograms – are safe, effective alternatives to Emerade 500 microgram.

Further advice for patients with an Emerade 500 microgram auto-injector is provided on page 8. Information is provided on the activation failures along with advice on how to handle an emergency event should a pen fail to activate and how to tell whether this has occurred by inspection of the pen. Healthcare professionals are urged to share this information with all patients and carers who have been prescribed an Emerade 500 microgram auto-injector

It is important to report all suspected adverse reactions or product quality defects via the Yellow Card reporting tool, www.mhra.gov.uk/yellowcard - patients and carers should be advised to retain the pen for further testing if possible.

Contacts for Further Information:

For stock enquiries please contact Bausch & Lomb Customer Services**,** Tel: 020 8781 2991
Email: Pharma_CS@bausch.com

For medical information enquiries please contact the Pharmacovigilance and Medical Information Officer, Tel: 0208 781 5523, Email: Pharmacovigilance.UK@bausch.com

Recipients of this Drug Alert should bring it to the attention of relevant contacts by copy of this letter. NHS Regional Teams are asked to forward this alert to Community Pharmacy, Dental and Optometry contractors and to any GP Practices within their regions that are not yet registered with the Central Alerting System (CAS).

Yours faithfully

Defective Medicines Report Centre
10 South Colonnade
Canary Wharf
London E14 4PU
Telephone +44 (0)20 3080 6574

Advice for patients with an Emerade 300 microgram auto-injector.

- Contact your doctor (via telephone, where appropriate) now to get replacements for you or your child's 300 microgram Emerade auto-injector(s) - also referred to as Emerade pen(s).
- Once you have two replacement pens in a different brand, return your Emerade 300 microgram pen(s) to a pharmacy, even if they are still in date - this should not require someone who is self-isolating to leave their home and pens can be returned at a later date.

According to our records, you or your child has been prescribed Emerade 300 microgram auto-injector (Emerade pen). The UK's regulator of medicines (Medicines & Healthcare products Regulatory Agency [MHRA]) has received updated information from the company that makes Emerade pens about the defect previously reported by the MHRA. The defect means some pens may fail to activate and therefore will not inject adrenaline. Recent results from tests on unused pens returned by patients indicate that approximately 13% of pens (13 in 100) need higher than normal force to activate. This implies a higher risk of failure to activate than was previously estimated. The earlier tests were conducted on pens that had not been carried by patients but had been stored in the manufacturing facility.

You, and/or your parent or carer, should make an urgent appointment with your doctor. Where possible, telephone appointments should be considered, based on the current UK Government guidelines for self-isolation, social distancing and shielding in relation to Coronavirus (COVID-19) – please follow the advice of your local GP practice/hospital and only attend where you are instructed to do so. Further information can be obtained on the government website: https://www.gov.uk/government/topical-events/coronavirus-covid-19-uk-government-response.

You will need a new prescription to replace each Emerade 300 microgram pen with one new adrenaline pen in an alternative brand up to a total of two adrenaline pens. The alternative pen will be either EpiPen or Jext, both of which are safe and effective in the treatment of anaphylaxis (severe allergic reactions). As soon as you have obtained two new replacement pens you should return your Emerade 300 microgram auto-injector(s) to a local pharmacy. If you are unwell or unable to collect your prescription because you have been asked to stay at home, please consider alternative arrangements to ensure that you receive your new pen(s), such as a family member collecting the prescription for you.

You and the people around you will need to ensure you know how to use your new EpiPen or Jext pens. They are used differently from Emerade. Ordinarily, your doctor, nurse or pharmacist would be able help you with training in how to use your new pen. However, we recognise that it may not be possible for you to visit your doctor or pharmacist at the present time. You and those around you must therefore take particular care to read the instructions on how to use your new pen in the leaflet contained in the box. You should also consult the manufacturer's website for the particular pen you have been supplied with. Training videos on how to use the pens and other information are available on these websites.

- EpiPen website epipen.co.uk and leaflet https://www.medicines.org.uk/emc/product/4290/pil
- Jext website jext.co.uk/ and leaflet https://www.medicines.org.uk/emc/product/5747/pil

The manufacturers will also provide training pens that do not contain adrenaline. You are strongly recommended to order these, and practise regularly with them, so you are fully prepared for use of a real pen in an emergency. Ensure you or your child knows to carry two adrenaline pens at all times.

What to do if you suspect anaphylaxis

- use your adrenaline pen immediately or ask someone else to do this if you prefer (any person is legally allowed to administer adrenaline to another person to save a life);
- call an ambulance (999) immediately after giving the injection or ask someone to do this. Say this is an emergency case of anaphylaxis (pronounced "anna-fill-axis"); use your second pen 5 to 15 minutes after the first pen if you are not improving or if you start to deteriorate after an initial improvement;

You can help us by continuing to report any issues directly via the Yellow Card reporting tool, www.mhra.gov.uk/yellowcard. Always include details of the brand and batch number on your pen.

Advice for patients with Emerade 500 microgram auto-injectors

According to our records, you have been prescribed Emerade 500 micrograms auto-injector (Emerade pen). The UK's regulator of medicines (Medicines & Healthcare products Regulatory Agency [MHRA]) has received updated information from the company that makes Emerade adrenaline pens.

There is a defect with some Emerade pens. In some cases, the needle is not released, and the injection of adrenaline is not delivered. You may have heard about this previously. You are now being informed that the risk is higher than previously thought. Recent results from tests on unused pens returned by patients indicate that approximately 13% of pens (13 in 100) need higher than normal force to activate. This implies a higher risk of failure to activate than was previously estimated. The earlier tests were conducted on pens that had not been carried by patients but had been stored in the manufacturing facility. The increased risk means it is even more important to follow the advice below.

Most pens will continue to work; carry two pens and use them if you need to
At this time there are not enough adrenaline pens of alternative brands to replace all the Emerade 500 microgram pens held by patients. Most Emerade pens will continue to work. Therefore, the risk to you of being left without any adrenaline from not having a pen is higher than the risk that an Emerade pen you are carrying may not activate. You must always carry two adrenaline pens with you and use them if you need to by following the instructions (see next page). If your first Emerade pen does not activate despite firm pressure, immediately use your second pen. If you are not improving and need a second dose of adrenaline, keep trying to activate a failed Emerade pen while waiting for the ambulance. Further notifications will be issued with immediate effect, as soon as supplies of alternative brands are able to meet the demand for replacement of the remaining Emerade pens held by patients.

Don't expose Emerade pens to heat
No brand of adrenaline pen should be exposed to temperatures higher than 25°C for prolonged periods. Avoiding high temperatures helps to maintain the adrenaline levels within the pen. Separately from this, there is a possibility that exposure to excessively high temperatures may increase the risk of activation failure with Emerade pens. Other causes apart from high heat are possible. However, as a precaution, you should protect your adrenaline pen from heat and do not leave your pen in a hot place (for example, in front of a heater, radiator, or fire.

When your Emerade pen expires, learn how to use your new type of adrenaline pen
When your Emerade pen is due to expire (the end of the month listed on the pen and case), you will be prescribed a different brand of adrenaline pen (EpiPen or Jext). There are some differences between how each brand is used. It is vital that you and the people around you know how to use the pens you have been supplied with.

Ordinarily, your doctor, nurse and pharmacist would be able to help you with training in how to use your new pen. However, we recognise that it may not be possible for you to visit your doctor or pharmacist at the present time. You and those around you must therefore take particular care to read the instructions on how to use your new pen in the leaflet contained in the box. The manufacturers of the different devices also have training information, including videos of how to use them correctly, on their websites. Trainer pens (mock pens that do not contain adrenaline) can also be obtained free of charge via the company websites. You are strongly recommended to order these, and to regularly practise with them. This will make sure you are fully prepared to use your real pen in an emergency. Further information can be found in the Patient Information Leaflets of the different pens and also on the respective manufacturers' websites where training videos are available.

- EpiPen Patient Information Leaflet - https://www.medicines.org.uk/emc/product/4289/pil
- Jext Patient Information Leaflet - https://www.medicines.org.uk/emc/product/5748/pil
- Emerade Patient Information Leaflet - https://www.medicines.org.uk/emc/product/5280/pil

If you have previously been prescribed Emerade 500 microgram, you can be reassured that EpiPen and Jext, both of which are available in a maximum strength of 300 microgram, are safe, effective alternatives to Emerade 500 microgram. You therefore do not need to replace each Emerade 500 microgram pen you used to carry with two 300 microgram EpiPens or 300 microgram Jext pens. You must still carry a total of two pens with you at all times – regardless of strength – in case you need to administer a second dose of adrenaline before the arrival of the emergency services.

What to do if you suspect anaphylaxis

- use your adrenaline pen immediately or ask someone else to do this if you prefer (any person is legally allowed to administer adrenaline to another person to save a life);
- call an ambulance (999) immediately after giving the injection or ask someone to do this. Say this is an emergency case of anaphylaxis (pronounced “anna-fill-axis");
- use your second adrenaline pen 5 to 15 minutes after the first pen if you are not improving or if you start to deteriorate after an initial improvement;
- use your second adrenaline pen immediately if an Emerade pen fails to activate despite pressing firmly against the thigh;
- if you are not improving and need a second dose, keep trying to use a failed Emerade pen while waiting for the ambulance, even if one pen has activated

A full investigation is still ongoing. The MHRA and Bausch and Lomb UK Limited will provide updated information to healthcare professionals and affected members of the public as soon as it becomes available.
You can help us by continuing to report any issues directly via the Yellow Card reporting tool, www.mhra.gov.uk/yellowcard. Always include the brand and batch number on your pen.

WHAT DOES MY EMERADE PEN LOOK LIKE BEFORE USE? Fig. 1



BEFORE USE

Instructions:

1. An unused Emerade pen, with front cap in place (Fig. 1).

2. For instruction on how to use your Emerade pen please consult the Patient Information Leaflet (PIL).

3. During this period, when activation failure is a possibility, you should press the Emerade pen very firmly against your thigh.

HAS MY EMERADE PEN ACTIVATED? Fig. 2



ACTIVATED
When Emerade Pen has been activated the needle cover will extend and lock.

Instructions:

1. After using an Emerade pen following the instructions found on product labelling, verify that the pen has activated.

2. An Emerade pen that has been activated, will have an extended needle cover (Fig. 2 – circled section of image)

3. Call 999 for an ambulance and state “Anaphylaxis” even if you start to feel better

4. Lie flat with your legs up to keep your blood flowing. However, if you are having difficulty breathing, you may need to sit up to make breathing easier

5. Proceed to administer your second pen if you are not improving after 5 to 15 mins in case you need a second dose of adrenaline

---

WHAT DO I DO IF MY EMERADE PEN HAS NOT ACTIVATED? Fig. 3



NOT ACTIVATED
If the needle cover has not extended, the pen has not activated.

Instructions:

1. If the needle cover has not extended, the pen has not activated (Fig. 3 – circled section of image).

2. If the pen has not activated despite firm pressure, use the second pen immediately.

3. Call 999 for an ambulance and state “anaphylaxis” even if you start to feel better.

4. Perform additional attempts to activate, if
- Both pens have failed, and no dose has been given;
- One pen has failed, one pen has worked, but a second dose is needed
This should only be attempted once all pens have been tried.

5. Retain any suspected, un-activated pen for reporting to the MHRA via the Yellow Card (further information on page 11) and investigation purposes.

Call for reporting

The reporting of suspected adverse drug reactions (ADRs) is of great importance. It allows continuous monitoring of the benefit-risk balance of a drug or medical device. Healthcare professionals and patients are encouraged to report any suspected defect or adverse event.

Please continue to report suspected ADRs to the MHRA through the Yellow Card Scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Card website - www.mhra.gov.uk/yellowcard or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- by downloading and printing a form from the Yellow Card website (see link above)

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.