LÆGEMIDDELSTYRELSEN
DANISH MEDICINES AGENCY

DKMA Update is an electronic newsletter intended for anyone who work with medicines either clinically or in the pharmaceutical industry or the retail industry and people who would like to gain an insight into our work and get the most recent updates on medicines and medical devices. The newsletter contains information about current medicine issues, the most recent safety updates and reimbursements.

DKMA Update

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Editorial: T cells – new perspectives in cancer treatment

By Nikolai Brun, MD and Director of Division of Medical Evaluation & Biostatistics

T cell therapy is the greatest breakthrough in modern cancer research. The technology opens up new and promising therapy forms, but it also changes the way we look at cancer in which we will see the immune response play a much greater role than previously.

In June, I participated in the Annual Meeting of the American Society of Clinical Oncology (ASCO), and one topic totally dominated the agenda: T cell therapy. Professionals call it CAR-T, which is an abbreviation for Chimeric Antigen Receptor.

A T cell is a type of white blood cell (leukocyte) which plays a central role in our immune system. T cells were on everybody's lips in Chicago, and several of the presentations I attended there could not have made it clearer: We are about to see a paradigm shift in cancer treatment.

T cell therapy is an extremely innovative therapy form whereby the cancer patient's own immune system is strengthened and engineered to attack the cancer cells. Research into T cells has been going on for several years, but it is only just recently that a real breakthrough has happened. In T cell therapy, some of the patient's own immunologically active T cells are removed and sent to a company that can manipulate the cells genetically. The company engineers the patient's T cells and tweaks them to target the specific type of cancer that the patient suffers from. The cells are then grown, which means

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they are allowed to multiply to form a far greater number of cells. The manipulated cells are then sent back to the hospital where the patient will have his or her own but now manipulated and multiplied cells infused into the bloodstream. It triggers a powerful immune response intended to make the patient's own immune system kill the cancer cells by artificially enhanced strength.

The results that I was presented with in Chicago showed an unprecedented response rate in very advanced cancer forms. And such a response rate *is* a breakthrough.

The preliminary studies of T-cell therapy show that up to 90% (in some studies up to 95%) of patients achieve complete remission of their disease. It means that many patients may benefit substantially from the treatment, also in relation to the possible adverse reactions – and in relation to the current treatment forms.

When the conference was held in June, the treatment had not yet been approved anywhere. However, this summer the U.S. Food and Drug Administration, FDA, approved the first drug for the treatment – and many drugs have been submitted to the authorities for assessment both in the USA and in Europe.

But even though the technology is fascinating and easy to be excited about, it also presents a large number of serious risks that we as authorities and doctors in clinical practice will need to consider when we assess the new treatment and decide whether to offer the new treatment to patients.

Most essentially, we must pay attention to the fact that it is the patient's own immune system that is being manipulated, which entails a risk that the treatment may cause serious adverse reactions in the form of a so-called 'cytokine storm'. This reaction is similar to a massive allergic reaction. The body attempts to reject the cells, and the reaction may last for several weeks with a potentially fatal outcome in 3% of patients.

For this reason, the assessment of the treatment's benefit-risk balance undertaken by the European Medicines Agency, EMA, is absolutely essential to ensure that the patients likely to be offered the treatment are selected carefully.

The first cancer disease that the FDA has approved the treatment for is acute lymphoblastic leukaemia (ALL) in children and adolescents. It involves a patient group having experienced a relapse of their disease for whom a cure with conventional means such as high-dose chemotherapy and bone marrow transplant is not possible.

It is expected that we will soon see more applications for several of the other types of blood cancer and for other types of leukaemia and lymphatic cancer. All these studies have moved to phase 3 already, and the timeline is thus 1-2 years. The therapy form is also investigated in other cancer forms, such as lung cancer and breast cancer. These studies are in phase 2, which means applications may be expected within approx. 3 years.

The DKMA is looking forward to following the EMA's work with assessing the companies' applications and concrete data as well as the new questions that will arise as a result thereof. For if the results hold true, we will be witnessing a paradigm shift in cancer treatment. The treatment supports modern times' scientific view on cancer that cancer should be considered as a disease caused by an imbalance in the immune system. This, in turn, suggests that from the perspective of prevention, we should step up efforts to minimise any behaviour that could impact the immune system negatively, such as smoking.

In parallel, the treatment raises a number of questions related to finances, interfaces and the division of work. In its present form, the treatment takes place by sending the patients' T cells to a company for manipulation. But theoretically, a certified blood bank with haematological specialist equipment and expertise would be able to perform the same type of task. The treatment could then be given faster, and transportation of the cell material would be unnecessary, but even so this could be obstructed if some companies have taken out patents for some of the methods.

At the DKMA we have no doubt that the technology itself is a potential turning point. We will be following the area with great excitement and will contribute constructively in the debates about risks, economic consequences and inter-disciplinary coordination that will be needed if the treatment is to be implemented in Denmark.

More opioids subject to stricter monitoring (dispensing status A§4)

The dispensing status of a number of opioids will be changed to A§4, which means the vast majority of opioids now have the same dispensing status.

The DKMA has decided to change the dispensing status of a number of opioids so that all opioids get the dispensing status of A§4 – with the exception of codeine combination products. The decision is supported by the Medicinal Products Committee.

When a medicine is given the A§4 dispensing status it means it is subjected to special monitoring, for example if it contains euphoriant substances (narcotic drugs and psychotropic substances), or if it is associated with a risk of abuse and dependence.

The medicines that already have the A§4 dispensing status today are those containing morphine, fentanyl, hydromorphone, methadone, ketobemidone, nicomorphine, oxycodone, pethidine, sufentanil and tapentadol. This list will soon be added with medicines containing buprenorphine, codeine, nalbuphine, opium as well as tramadol that will get the A§4 dispensing status.

The decision to change the dispensing status has been announced to the marketing authorisation holders, who may object to the effective date of the dispensing status. We expect the process to be completed by end-October following which the exact effective date of the dispensing status will be announced.

In practice, the change of dispensing status implies that the prescribing patterns of doctors can be monitored because the prescription can be linked to the doctor's provider ID, digital signature or civil registration number (CPR number).

The change in dispensing status is prompted by a steady increase in the consumption of opioids over the recent years. The risk of developing abuse or dependence applies to the entire drug class. The dependence potential may vary between the individual opioids, but the DKMA and the Medicinal Products Committee generally assess that all opioids could lead to dependence if given in sufficiently high doses and for prolonged periods in particular. The DKMA has therefore decided to harmonise the dispensing status of opioids.

The change covers only opioids authorised for human use. Opioids for veterinary use are not included.

Specifics about each medicine

Buprenorphine
Buprenorphine is a partial agonist that could be abused, and it may produce dependence. All buprenorphine products are therefore now assigned the A§4 dispensing status.

Codeine
Codeine is metabolised into morphine, its active opioid metabolite. 25 mg of codeine corresponds to 2.5 mg of morphine. Codeine may therefore cause the same dependence as morphine – it is simply a question of dosage. Codeine therefore changes its dispensing status from A to A§4.

Combination products
The risk of abuse of combination products like Kodipar® and Kodimagnyl® is estimated to be lower since the content of paracetamol and acetylsalicylic acid, respectively, will limit how much codeine it is possible to consume without also taking a toxic dose of paracetamol or acetylsalicylic acid. This means that no change in dispensing status is recommended for combination products. The combination products cannot cause dependence as the substance they are combined with will lead to toxicity before any such dependence would occur.

Nalbuphine
Nalbuphine is only available for injection and has kappa-agonistic and mu-antagonistic properties. Although the abuse potential is described as being very low, abuse of nalbuphine can lead to psychological and physical dependence. For this reason, the dispensing status is changed from A to A§4.

Opium
Opium is contained in an oral solution in “Pectyl brystdråber” (cough suppressant) and “Pectyl stærke brystdråber” (strong cough suppressant). Opium is also contained in Opium ”NMI” oral drops which has dispensing status A§4. Pectyl is a combination product and in addition to camphor it contains alcohol corresponding to approx. 34-42.7 vol%, i.e. up to 1389-1725 mg per dose depending on the product. Opium contains a number of different alkaloids, including codeine and morphine that have agonistic effect on the opioid receptors. The recommended dosage corresponds to about 1 mg of morphine per dose, and this entails a risk of dependence. Doses are recommended 2-5 times daily. For this reason, the dispensing status for opium is changed from A to A§4.

Tramadol
Tramadol is a synthetic opioid. Based on the last 10 years' continuously rising consumption of tramadol, the dispensing status is changed from A to A§4.

Medicinal cannabis – new products, new rules and new guidelines

Medicinal cannabis is a hot issue at the Danish Medicines Agency this autumn. We are preparing new guidelines for the medicinal cannabis pilot programme and will be reviewing applications from Danish producers that would like to produce cannabis for medicinal use.

On 1 January 2018, the medicinal cannabis pilot programme is planned to start; this means that Danish doctors will be able to prescribe a new type of cannabis products that are not authorised medicinal products and have not previously been available on the Danish market. It has not yet been decided which specific cannabis products will be available at pharmacies. The range of products will depend on which products import businesses decide to import and what can be produced in Denmark.

The medicinal cannabis pilot programme requires the adoption of new legislation presented to the Danish Parliament on 5 October 2017. At the same time as the new legislation comes into force on 1 January 2018, a number of executive orders and guidelines for the pilot programme will take effect.

Guidelines for doctors on the way

The first draft of the guidelines for doctors was submitted for consultation during the summer. The draft was prepared on the basis of international scientific evidence in this field. Since there is only limited evidence of efficacy, adverse reactions and interactions caused by medicinal cannabis, we have drawn inspiration from other countries and from applications for compassionate use permits for Marinol and Nabilone that we have reviewed over the years.

The Danish Medicines Agency received 20 consultation responses to the guidelines, and we are currently working on a consultation note that we expect to publish on the Danish consultation portal (Høringsportalen) in October. The final guidelines will be completed when the new legislation for the medicinal cannabis pilot programme has been adopted.

As regards adverse reactions, an executive order on the reporting of adverse reactions from medicinal cannabis and the processing of adverse reaction reports was recently submitted for consultation. The consultation deadline is 26 October 2017.

Executive order on the import of cannabis products

The pilot programme also requires a new executive order specifying the rules on import and distribution of cannabis products for the pilot programme. The import of cannabis products requires an import authorisation from the Danish Medicines Agency, and the requirements for obtaining authorisation to manufacture intermediate products appear from the executive order. This executive order has been submitted for consultation along with the guidelines and application form, and the consultation deadline is 20 October 2017.

The application form and the guidelines were published on the Danish Medicines Agency's website on 29 September 2017. Thus, businesses can now apply for authorisation to import cannabis primary products and manufacture cannabis intermediate products. However, authorisations will not be valid until 1 January 2018 when the rules become effective.

Guidelines on the cultivation of medicinal cannabis
Simultaneously with the medicinal cannabis pilot programme, the Danish government has decided to make it possible for Danish businesses to cultivate and develop cannabis suitable for medicinal use.

The Danish Medicines Agency is responsible for issuing medicinal cannabis cultivation licences in Denmark; a task we carry out in collaboration with the Danish National Police and the Danish Agricultural Agency.

This is the *Development scheme for the cultivation and handling of cannabis for medicinal use*. According to the guidelines, businesses applying for a medicinal cannabis cultivation and production licence must aim to develop standardised products. They are required to demonstrate that the content of active substances is the same from one harvest to another and that they maintain full control over their production processes. This is essential for patient safety. Cultivation must be in accordance with the guideline on good agricultural and collection practice (GACP) and good manufacturing practice (GMP), and process analyses must be made to show that the practice is complied with. For example, cultivation should take place indoors in enclosed spaces with the right amount of light, water etc.

The application form and the guidelines for the application were published on the Danish Medicines Agency's website on 29 September 2017. Thus, businesses can now apply for a medicinal cannabis cultivation and production licence. However, licences will not be valid until 1 January 2018 when the scheme becomes effective.

Public funds for research in medicinal cannabis
The Danish Parliament has earmarked DKK 5 million from the special funding scheme for research projects for the purpose of collecting scientific experience for the pilot programme.

The specific criteria for applications for the funds will be published on the website of the Danish Medicines Agency as soon as the proposal has been presented to the Danish Parliament.

Projects applying for the funds must describe the purpose of the project in detail and the relevance in relation to the overall purpose of the pilot programme, which is to gather knowledge about the use of medicinal cannabis – including any patient safety consequences. The projects may be carried out as randomised clinical trials, case control studies, interaction studies, or studies elucidating the use of cannabis products compared with conventional treatment etc.

As part of the decision on the allocation of funds, the Danish Medicines Agency will send applications received on time to Innovation Fund Denmark. Innovation Fund Denmark makes a peer review of the applications received. The applications deemed worthy of support by Innovation Fund Denmark will be prioritised by a reference group. The reference group will make a recommendation for the prioritisation to the Danish Medicines Agency. The Danish Medicines Agency will then make a recommendation to the Danish Ministry of Health, which will make a decision as to the distribution of the research funds.

Professional debate on medicinal cannabis
As we are getting closer to the start date of the pilot programme, we will invite relevant stakeholders to a professional debate on medicinal cannabis. The debate will be held in our canteen and healthcare professionals and other stakeholders will be given the opportunity to ask specific questions about the pilot programme.

New 9-valent HPV vaccine in the childhood immunisation programme

From 1 November 2017, 12-year-old girls will be offered a new and more effective HPV vaccine in the childhood immunisation programme when the Cervarix® HPV vaccine is replaced by Gardasil®9. The switch is made in pursuance of the statutory vaccine tender.

When the new Gardasil®9 HPV vaccine is included in the childhood immunisation programme, vaccinated girls will be protected against 90 per cent of the HPV types that may cause cervical cancer. As the name suggests, Gardasil®9 is a 9-valent vaccine. This means it contains antigens from nine HPV types: 6,11,16,18,31,33,45,52 and 58. Antigens make the body produce antibodies against virus. The three HPV vaccines, Cervarix®, Gardasil® and Gardasil®9, all contain antigens from the HPV types 16 and 18, which cause approx. 70 per cent of all cervical cancer cases. Gardasil®9 is the only one of the three HPV vaccines that contains also antigens from the HPV types 31, 33, 45, 52 and 58, which combined cause a further 20 per cent of cervical cancer cases. Gardasil® and Gardasil®9 also contain antigens from the HPV types 6 and 11, which may cause genital warts.

Evidence base for the efficacy of Gardasil®9
Besides cervical cancer and precancerous cervical conditions, Gardasil®9 is authorised for the prevention of cancers affecting the anus, vulva (vaginal opening) and the vagina. The vaccine is authorised for girls and boys from the age of 9 years.

In the eight clinical studies based on which Gardasil®9 was authorised, the vaccine is compared with the previous Gardasil® vaccine, which was supported by solid studies which have already shown a preventive effect against HPV infection and precancerous conditions. These comparable studies have shown that the Gardasil®9 vaccine is just as effective as Gardasil® in relation to the four HPV types 6, 11, 16 and 18, and in addition it offers protection against the HPV types 31, 33, 45, 52 and 58.

One of the studies, which enrolled 14,204 women aged between 16 and 26 years, investigated how many developed cell changes related to the five additional HPV types 31, 33, 45, 52 and 58. The study looked at the 12,033 women who were not already infected with the five HPV types before the first vaccination. 6,016 of the women received Gardasil®9, while 6,017 women received Gardasil®. After 5½ years, one woman in the Gardasil®9 group had developed precancerous conditions caused by one of the five additional HPV types. Among the women receiving Gardasil®, 38 of them had developed precancerous conditions.

To find out for how long the vaccine is effective, the persons vaccinated with Gardasil®9 in the clinical studies are monitored for 10 years. It is examined if the antibodies against HPV persist and whether precancerous conditions develop. The preliminary results after three years of monitoring show that the vast majority are still protected against the nine HPV types.

Known adverse reactions to Gardasil®9
The adverse reactions reported in the course of the clinical trials of Gardasil®9 are the same as those reported for the other HPV vaccines Cervarix® and Gardasil®.

The most commonly observed adverse reactions were reactions at the injection site and influenza-like symptoms such as headache, fever, fatigue, pain, dizziness and nausea. The reactions are often mild and transient.

The clinical trials of Gardasil®9 reported more cases of local reactions at the injection site with redness and swelling compared to Gardasil®. The number of reported serious adverse reactions were the same for the two vaccines.

Like many of the other vaccines in the childhood immunisation programme, Gardasil®9 contains an aluminium adjuvant. An adjuvant is an excipient that increases the efficacy of a vaccine. The risk of local reactions at the injection site such as soreness, swelling and redness increases with the amount of aluminium in the vaccine. Gardasil®9 contains more aluminium than Gardasil®, but contains the same amount of aluminium as Cervarix®.

When an adjuvant is added to the vaccine, fewer vaccinations and a smaller amount of antigen are needed.

Aluminium has been used as an adjuvant since the 1930s, and drug regulatory authorities around the world consider it effective and safe, but it is a well-known fact that aluminium in vaccines may cause a local reaction at the injection site.

Stricter reporting requirements
From 1 November 2017 when Gardasil®9 is included in the childhood immunisation programme, it will be subject to stricter reporting requirements implying that suspected adverse reactions must be reported for a period of two years just like any other new medicine. This means that any suspected adverse reactions associated with the vaccine must be reported by doctors. After the two years, doctors are required to report all serious or unknown adverse reactions suspected to be caused by Gardasil®9.

The DKMA encourages other healthcare professionals as well as vaccinees and their relatives or representatives to report suspected adverse reactions to the DKMA. When reporting an adverse reaction, it is important to remember to indicate the name of the administered HPV vaccine and its batch number if possible.

Read more about the changes affecting HPV vaccination in the childhood immunisation programme in the latest issue of EPI-NEWS from SSI.

Adverse reactions can be reported to the DKMA at www.meldenbivirkning.dk (report a side effect).

The DKMA is expanding and recruiting new employees

The DKMA is currently expanding its activities and is looking for new medical employees. The positions to be filled are medical positions within a number of clinical specialities for the new Medical Evaluation & Biostatistics Division headed by Nikolai Brun (NB).

Why are you recruiting so many employees right now?
NB: ”Brexit has triggered extra tasks for the remaining agencies in the EU. In this respect, we have to handle increasing volumes of work. It fits perfectly with the strategy announced by the Government’s Growth Team for Life Science earlier this year. A medicines agency that is among Europe’s best in class is considered one of the most important means to ensure growth for Danish life science. So, this is a very exciting time for us as we start to expand our assessment and supervision teams considerably. It will ensure that we can play a greater role on the European scene in the foreseeable future.”

What development is otherwise characterising the Danish Medicines Agency right now?
NB: “Since the Danish Medicines Agency was re-established as an independent agency in 2015, we have been working to position ourselves in a European context. Denmark has a sound health service, a strong research environment and a large life science industry with many biotech start-ups, but historically we have probably had a regulatory authority on a somewhat smaller scale. We are changing this now by strengthening the Danish Medicines Agency. What’s interesting about the industry is that it will actually be reinforced by having a national authority that is deeply rooted in European affairs. It stimulates growth and ensures timely and competent counselling in the early stages of the development of new medicines.

What specific tasks will grow in number?
NB: “It will be a broad range of tasks that are all related to existing and especially new medicinal products. We are seeing tremendous growth in the number of new medicinal products submitted for approval within a line of fields that are in great need of new treatment options. So, this is a favourable opportunity to influence which medicinal products are to be offered in the future’s medical treatments. In a European context, we have a unique opportunity to leave a Danish imprint on the development right now.”

What qualifications are you looking for?
NB: "We need classical clinical pharmacologists, who still represent a large share of the agency, but doctors with a broader background in internal medicine may also be considered. We are also seeing considerable growth in tasks within the field of cancer, so we are looking for haematologists as well as oncologists. Medicines for diseases of the central nervous system are also demanding more and more hands, so doctors with credentials in neurology, neurophysiology or biological psychiatry, etc. can certainly make a difference with us. We are trying to create a work environment with rich diversity and different skills. Personally, I am very impressed with the wide variety of skills already in the organisation, but I also see that we can stimulate this further by recruiting an even more

diverse workforce of also international employees. As I see it, diversity will substantially strengthen both innovation and creativity in the individual teams".

Will you only be hiring if EMA relocates to Denmark?
NB: “No. Whether Copenhagen will host EMA or not is really not essential in this respect. It would be very welcome of course, and it would help stimulate Danish drug development even further, but our daily work is entirely independent of this process. We recently formulated an ambitious strategy to position the Danish Medicines Agency among Europe's best in class. It already drives our daily work in everything we do each and every day. It is simply where we want to be within the next five years. Obviously, this is only possible for a workplace among the very best, and we therefore want to become Denmark's best workplace. When we go to work every morning, it must be with a smile on our faces and a passion for both national and European work.

What can you offer your employees?
NB: "We can offer our employees by far the most exiting work within the pharmaceutical area at present. Even though the highest wages are found elsewhere in the industry, we offer really good work conditions. For example, we do not have night shifts even though we travel to colleagues around the world. We have already received many applications from contenders who are interested in our positions, so there is no time to waste if you want to join Denmark's best workplace."

Watch the Danish movie: The Danish Medicines Agency as a place to work.

New report on biological medicines and biosimilars

In a new report, the DKMA reviews reports on suspected adverse reactions to selected biological medicines and biosimilars. Based on the ADR reports, there is no indication that the profiles of adverse drug reactions of biosimilars and their reference medicinal products, respectively, differ from one another.

In spring 2017, the DKMA published its first report on selected biological medicinal products and biosimilars as part of an action plan for better monitoring of biological medicines[1]; *ADR reports on and consumption of selected biological medicinal products (*Danish title: *Bivirkningsindberetninger om og forbrug af udvalgte biologiske lægemidler).* The report showed that there were no signals of safety concerns for the selected biological medicines or biosimilars. Because new biological medicines and biosimilars are put on the market regularly, it was decided that strict monitoring of adverse reactions of these biological medicines was still to be a focus area for the DKMA in the future.

As a result, the DKMA has prepared this new report, which reviews the consumption and ADR reports for the period 1 January to 30 June 2017: ADR reports on and consumption of selected biological medicinal products (Danish title: *Bivirkningsindberetninger om og forbrug af udvalgte biologiske lægemidler*). Based on the reported suspected adverse reactions, there is no indication that the profile of adverse reactions of the reference medicinal products is different from the profile of adverse drug reactions of the biosimilar versions. No signals of safety concerns have been detected for the selected biological medicinal products.

Consumption data show that the Danish regions have followed the recommendations from the Danish Medicines Council to switch from Remicade to Remsima and from Enbrel to Benepali. In the first six months of 2017, Remsima accounted for 98% of the consumption of infliximab-containing medicines, and Benepali accounted for 79% of etanercept-containing medicines.

The report also shows that doctors have recorded the batch numbers in approx. two thirds of the ADR reports, which is an increase compared to previous reports. Especially in the ADR reports on Benepali and Remsima did doctors provide a batch number in the original report, or the DKMA was able to retrieve the batch number subsequently.

[1]Action plan on better monitoring of biological medicines, biosimilars and vaccines for 2015-2016 (Danish title: *Handleplan om bedre overvågning af biologiske lægemidler, biosimilære lægemidler og vacciner 2015-2016*).

Global operation against illegal medicines

More than 25 million units containing potentially life-threatening medicines were seized and more than 3,500 websites were taken offline or had their payment facilities removed for illegal sale of medicines during Operation Pangea.

Operation Pangea is a global operation against the illegal sale of medicines. The operation took place this year from 12 to 19 September 2017 with participation from the police, tax and customs authorities and drug regulatory authorities from 123 countries.

The WHO and the European Alliance for Access to Safe Medicines estimate that more than half of the medicines sold globally are falsified or sold illegally. It poses a huge risk to patients all over the world, and it challenges the authorities because the black markets are profitable.

At the DKMA we are taking these issues very seriously and have just completed an information campaign about illegal medicines to advise Danes who buy medicines online to look for the green EU logo that is only displayed by authorised shops. We have also run a social media campaign together with the Danish Association of the Pharmaceutical Industry where we have tried to strike the right balance between seriousness and humour. Under the hashtags #ulovligmedigrin and #ulovligmedicin on Twitter, you can find more information and support our messages (information is in Danish).

Link to Facebook: https://www.facebook.com/laegemiddel/

Link to #ulovligmedigrin https://twitter.com/search?q=%23ulovligmedigrin&src=typd

Most recent Direct Healthcare Professional Communications (DHPCs)

Below is a list of the most recent DHPCs that have been sent out to relevant doctors and healthcare professionals with safety information and updated recommendations about medicines:

- **Dacogen (decitabine)**: Dacogen 50 mg, powder for concentrate for solution for infusion – Change in the recommendations for diluting reconstituted Dacogen solution. Sent out September 2017.
- **Human epoetins**: New warnings about serious cutaneous adverse reactions. Sent out 21 September 2017.

The DHPCs are available at the DKMA website – most of them in Danish only: Direct Healthcare Professional Communication (DHPC) sent to healthcare professionals.