

Fertility treatment 'add ons'

Strategic delivery: Setting standards Increasing and informing choice Demonstrating efficiency economy and value

Details:

Meeting Authority

Agenda item 9

Paper number HFEA (18/01/2017) 823

Meeting date 18 January 2017

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Output:

For information or decision? For decision

Recommendation

- Members are asked to discuss the questions in section 3.7 and consider the proposed next steps.

Resource implications Minimal expenditure in information phase, beyond IfQ costs

Implementation date Different phases listed in section 4

Communication(s) Milestones at section 4. Separate communications plan to be developed.

Organisational risk Low Medium High

Annexes Annex A: Add ons, their efficacy and their cost
Annex B: Code of Practice guidance for clinics on patient information

1. Background

- 1.1. As the specialist regulator of fertility treatment, we want patients to have access to high quality care – and that means high quality information and preparation for treatment, as much as it means the treatment itself. This ambition is central both to our 2014-17 strategy and to our strategy for 2017-2020, endorsed at today's Authority meeting.
- 1.2. Patient demand for good information has never been higher, a demand we are meeting through our new website, due to launch in the spring. Patients have expressed a particular desire for information about adjuncts to their fertility treatment, known as 'add ons'. Whilst being open to new treatments, patients have reported feeling confused and overwhelmed by information about add ons; whether they are safe and effective and, therefore, worth paying the additional amount that clinics often charge for them.
- 1.3. Many clinics in the UK offer add ons and their use seems to be on the rise. Innovation can of course be a force for good, yet many clinicians and scientists working in or around the field question the evidence for the safety and efficacy of many add ons, arguing that, for most add ons, there is no evidence that they increase the chance of a pregnancy or birth and, for some, there is a concern about the possible side-effects.
- 1.4. We have had concerns about the apparent proliferation of fertility treatment add ons for some time. Prompted by concerns and questions raised by patients and with advice from our Scientific and Clinical Advances Advisory Committee (SCAAC), we have produced clear, honest information for patients about add ons; how safe they are, whether they work to increase pregnancy and birth rates, and how much they are likely to cost.
- 1.5. In this paper, we set out what add ons are, what work we have done and are planning in this area, and what steps we might take next to encourage a more responsible attitude towards innovation in the sector and improve the situation for people having fertility treatment.

2. What do we know?

- 2.1. Fertility treatment add ons are additional therapies and techniques which are claimed to increase the chance of pregnancy and birth from IVF or other fertility treatments. Some add ons have been offered for some years while others are more recent developments.

2.2. There is some debate about what should be regarded as an add on¹. However, SCAAC has identified nine add ons as a first batch that patients most need information about (see annex A for an explanation of each one). They fall into four broad categories:

- Surgical procedures:
 - endometrial scratching
- Drug therapies:
 - reproductive immunology treatment (steroids, intravenous immunoglobulin, TNF-a blocking agents and intralipid infusions)
- Embryological techniques:
 - egg activation with calcium ionophore
 - intrauterine culture
 - embryo glue
 - elective freeze-all
 - assisted hatching
 - preimplantation genetic screening
- Laboratory equipment:
 - time-lapse imaging

2.3. Our own review of clinic websites carried out in August 2016² found that:

- 70% of all licensed clinics offer at least one add on
- patients are more likely to be offered an add on at a London clinic than elsewhere in the UK
- some clinics offer add ons free of charge, but most are offered at additional cost
- prices for the same add ons vary enormously from one clinic to the next
- there is also variation in the information offered to patients about add ons, with some clinics being less open than others about the lack of evidence of effectiveness. This is something that was backed up by a recent study in the BMJ.

2.4. SCAAC has reviewed the scientific literature on these add ons and discussed patient information for the new website at its February and June 2016 meetings. The committee has developed a traffic light rating to show clearly how strong the evidence of efficacy is and this rating is being independently

¹ A recent paper in the BMJ looked at claims on clinics' websites regarding 41 fertility interventions in addition to IVF and ICSI. There has been some debate about whether these interventions are all add ons, given they include established procedures such as sperm freezing and frozen embryo transfer

² We searched the websites of the 125 centres which were licensed at that time for 10 treatment add ons (this included DNA fragmentation, which is not one of the nine add ons about which we will have information on the first iteration of the new HFEA website). Of those, 87 clinics offered at least one of the 10 add ons.

validated at the moment. Only one add on currently has a green rating (ie, that there is good evidence of that it improves success rates).

- 2.5.** We have lots of feedback from patients about treatment add ons over the past few years, some in the context of our strategy and some around information for the new website. Our most recent survey of patients, regarding priorities for the 2017-2020 strategy, elicited the following comments from current or former patients about why they thought clarity about the evidence for (or against) the effectiveness of different treatments and treatment add ons was important:

'Clarity about different add on treatments. At the clinic I've had treatment at, even the staff have vastly differing opinions about what I should and shouldn't bother having done which is frustrating.'

'More information about add ons and the science behind them.'

'I would like to see add ons and their effectiveness clearly explained.'

'Openness and honesty about effectiveness of add-ons.'

- 2.6.** A recent episode of the BBC's Panorama programme covered the issue of treatment add ons, focussing on reproductive immunology, PGS and time-lapse imaging. The programme has variously been described as an unfair depiction of IVF in the UK and as a missed opportunity, in that it failed to give a true picture of the extent of the use of add ons in the sector. Whatever one's view, it certainly raised the issue with a wide, public audience.

- 2.7.** In summary, these reviews and patient feedback suggest the following:

- Add ons are offered in many clinics, often at additional cost
- Many add ons do not have a strong evidence base to show their effectiveness
- Many clinics are not making it clear to patients that the evidence of effectiveness is weak – some are even offered as standard treatments
- Patients are confused about the merits of different add ons and are not sure who to trust for information

3. How should we respond to this issue?

- 3.1.** Patients want accurate, update-to-date information about treatment add ons. They also want to be given safe and effective treatments at a reasonable price. They are open to new treatments and to trying out untested ones, but want to understand their limitations. A worrying development is that they seem to be losing faith in the sector, feeling that they are sometimes being ripped off.

- 3.2.** As noted above, we will be publishing information about nine add ons on our new website, available in spring 2017, and working with stakeholders to publicise it. But it is also worth thinking about:

- the information that clinics themselves publish and give to patients verbally

- how the add ons are offered to patients and charged for.

Information published by clinics

3.3. We publish guidance in the Code of Practice around information to be given to patients before they consent to treatment:

4.2 Before treatment is offered, the centre should give the woman seeking treatment and her partner, if applicable, information about...

(e) the likely outcomes of the proposed treatment (data provided should include the centre's most recent live birth rate and clinical pregnancy rate per treatment cycle, verified by the HFEA, and the national live birth rate and clinical pregnancy rate per treatment cycle)

(f) the nature and potential risks of the treatment, including the risk of children conceived having developmental and birth defects

(g) the possible side effects and risks to the woman being treated and any resulting child, including ovarian hyperstimulation syndrome (OHSS).

3.4. We also expect clinics to give each patient a costed, personalised treatment plan. Finally, we give guidance about the responsible use of websites. See annex B for full guidance in these areas.

3.5. The information guidance is focussed primarily on licensed fertility treatments, rather than add ons, and the websites guidance is aimed more at how birth statistics are presented. So, it may be worth reviewing our information requirements of clinics, to make sure that they are relevant to treatment add ons. As part of that work, we could look at best practice in publishing information about untested treatments, including advice from the Advertising Standards Authority.

How services are offered to patients

3.6. Ensuring that patients have access to good information about add ons – both from us and from clinics - will be an important step in addressing the inadequacies in the way in which many of them are offered. It will make patients feel more confident about discussing add ons with their clinic and more discerning about whether to opt for them. However, information alone may not be enough in itself to effect more radical change. A more complex question is what we might do as the regulator to improve the way that add ons are offered to patients in the clinic. And how might we approach add ons over which we have limited regulatory powers, such as surgical and drug therapies?

3.7. Some questions that arise:

- **Are there any add ons that clinics should not be offering at all, either because they are unsafe or demonstrably ineffective?**
- **If an add on is new, how should they be introduced into clinical practice: should we expect to see laboratory research and/or a clinical trial first?**

- **Where there is limited evidence of effectiveness, should clinics charge extra for add ons or provide it free of charge?**

- 3.8.** These are not questions necessarily to be answered today. Rather, they are suggested as discussion points for the Authority and, perhaps, the basis of a discussion with professionals and patients about what constitutes responsible use of add ons in the clinic. One strand of work might be to develop a consensus about responsible innovation in fertility treatment that we could agree with stakeholders and encourage clinics to sign up to. Our success with changing professional and patient attitudes towards single embryo transfer suggests that we could make some mileage through this style of collaborative working, coupled with an effective public education campaign.
- 3.9.** As we have found with the One at a Time campaign, such cultural change can be a very powerful tool for bring about the improvement we want to see. Such an approach may not bring all clinics on board, but it will increasingly isolate those who do not embrace the campaign's messages. We could, whilst we are testing the effectiveness of the campaign approach, explore the extent of our regulatory powers, particularly around laboratory equipment standards, clinical trials and advertising claims.

4. Summary and next steps

- 4.1.** Treatment add ons is not a straight forward issue. We do not want to create a situation in which innovation in fertility treatment is stifled. There may well be a place for treatment add ons in the clinic. However, we want patients to have access to good quality, reasonably-priced treatments which maximise their chance of a pregnancy and birth. There is an important role for us to play in achieving that goal.
- 4.2.** Besides offering good information and advice to patients - and encouraging clinics to do the same – we may also have a role to play in increasing the amount of research taking place around different add ons. This might be through analysis of our data or perhaps through encouraging clinics to carry out studies and publish their findings – all carried out through collaboration with scientific and clinical professional bodies, patient organisations and perhaps scientific publications.
- 4.3.** During 2017-18, we might want to:
- Launch the new patient information, backed up by an awareness campaign
 - Continue to monitor the scientific literature and listen to patient feedback
 - Work with professional societies, patient groups and interested clinics to develop a consensus around what responsible innovation looks like, potentially kicked off with a workshop at the annual conference in March
 - Extend the public awareness campaign to promote responsible innovation, encouraging clinics to sign up to the consensus statement and to offer add ons in that way

- Explore how we could encourage and perhaps facilitate research which adds to the evidence base for each treatment add on (and future ones).

4.4. Beyond 2017/18, we might want to:

- Monitor the impact of this effort, explore other regulatory levers and consider introducing further requirements if progress is slow.

4.5. Members are asked to discuss the questions in section 3.7 above and consider the proposed next steps.

Annex A: Add ons, their efficacy and their cost

Category	Add on	Description	Average price
Surgical procedures	Endometrial scratching	<p>Carried out before IVF, endometrial scratching is intended to correct problems with the womb lining. The lining of the womb is 'scratched' using a small sterile plastic tube.</p> <p>The theory is that this procedure triggers the body to repair the site of the scratch, releasing chemicals and hormones that make the womb lining more receptive to an embryo implanting.</p> <p>Early results suggest that endometrial scratching could increase pregnancy rates, although stronger evidence is needed to prove this.</p>	£210
Drug therapies	Reproductive immunology	<p>Reproductive immunology is a field of study that looks at how a woman's immune system reacts when she becomes pregnant.</p> <p>Some scientists believe that in some cases of miscarriage or infertility, the mother's immune system may fail to accept the embryo, in the same way that the body rejects transplanted cells or organs.</p> <p>Drugs regimes include steroids, intravenous immunoglobulin, TNF-α blocking agents and intralipid infusions.</p> <p>Not only does reproductive immunology treatments not improve pregnancy rates, there are risks attached to all these treatments, some of which are very serious.</p>	£671
Embryological techniques	Egg activation with calcium ionophore	<p>When a sperm meets an egg, it triggers a process called 'egg activation' which starts off the process of embryo development, while at the same time allowing only one sperm to fertilise the egg. If the egg doesn't activate, then it won't develop.</p> <p>Egg activation may be stimulated by chemicals called calcium ionophores. These chemicals can be added to the embryo in the lab.</p> <p>In theory, egg activation using calcium ionophores could cause embryos to have abnormal numbers of chromosomes, which would cause the pregnancy to miscarry. As yet there's not enough evidence to decide whether these risks are a serious concern.</p> <p>Given the possible risks, clinics offering this treatment are expected to do so only in selected patients who have had failed fertilisation and to justify their reasons for doing so.</p>	Unknown

	Intrauterine culture	<p>During a conventional IVF cycle, eggs are fertilised and allowed to develop in a special culture fluid inside an incubator. Intrauterine culture differs in that it allows the early stages of embryo development to take place within the patient's womb. The eggs are fertilised and placed in an intrauterine culture device, which is inserted into the woman's womb.</p> <p>The device stays in place for several hours during the initial stages of embryo development. When the device is removed, the embryos are put in an incubator until they are ready to be transferred back to the womb or frozen for use in future treatment.</p> <p>There's currently not enough evidence to show that intrauterine culture improves birth rates and is safe.</p>	Included in cost of IVF cycle – under clinical trial
	Embryo glue	<p>Embryo glue contains a natural substance called hyaluronan, which may improve the chance of the embryo implanting in the womb. It is added to the solution in the dish in which the embryos are kept before being transferred to the woman.</p> <p>Embryo glue has been shown to increase pregnancy and births rates by 10%.</p>	£171
	Elective freeze-all	<p>Elective freeze all cycles involve creating embryos using IVF and then freezing all of them so no embryos are transferred in the 'fresh' cycle. The embryos are thawed a few months later and transferred to the woman's womb as part of a frozen embryo transfer (FET) cycle.</p> <p>There is some evidence that the body's hormonal response to fertility drugs can affect the lining of the womb, which makes it more difficult for the embryos to implant. Freezing the embryos means they can be transferred back into the woman when the womb lining is well developed.</p> <p>It's also thought by having all their embryos frozen, women are at lower risk of suffering from ovarian hyperstimulation syndrome (OHSS), an overreaction to fertility drugs. This is because OHSS is more common and more severe when it occurs during a pregnancy. There is a clinical trial underway to determine whether it is safer and more effective.</p>	Included in cost of IVF cycle – under clinical trial
	Assisted hatching	<p>The egg and early embryo are surrounded by a thick layer of special proteins called the zona pellucida. Before an embryo can implant in the womb it has to break out or 'hatch' from its zona pellucida.</p> <p>Some people think that assisted hatching - using acid, lasers or other tools to thin or make a hole in the zona pellucida - helps the embryo to hatch.</p> <p>The NICE Fertility guideline says that assisted hatching has not been shown to improve pregnancy rates.</p>	£369

	PGS	<p>PGS involves checking embryos for abnormalities in the number of chromosomes. Embryologists remove a cell, or if at a later stage, several cells, from the embryo, which is then tested for any chromosomal abnormalities.</p> <p>There is no evidence to show that this type of PGS is beneficial for women over 37, couples who had had several miscarriages or failed IVF cycles, people with a family history of chromosome problems, and men whose sperm may carry abnormal chromosomes.</p> <p>Three small studies have now shown that PGS carried out at a later stage, the blastocyst embryo on day 5 or 6, might improve success rates in younger patients who are typically under 37 with no history of miscarriage or failed IVF cycles. However, more evidence is needed to confirm these findings.</p>	£2620
Laboratory equipment	Time lapse imaging	<p>Time-lapse imaging allows the embryologist to take thousands of images of the embryos as they grow without disturbing them. Not only does this mean the embryos do not have to be removed from the incubator, it also allows the embryologist to get a continuous view of each embryo as it develops, rather than just viewing them once a day.</p> <p>The embryologist can then choose a specific embryo for implantation based on criteria such as rate of development and the number and appearance of cells. Indeed, being undisturbed while they grow may improve the quality of the embryos.</p> <p>There have been various studies to try and see if time-lapse imaging can improve birth rates. Initial research has shown some promise, but it's still very early days.</p>	£672

Annex B: Code of Practice guidance for clinics on patient information

Information for those seeking treatment

4.2 Before treatment is offered, the centre should give the woman seeking treatment and her partner, if applicable, information about...

- (d) fertility treatments available
- (e) the likely outcomes of the proposed treatment (data provided should include the centre's most recent live birth rate and clinical pregnancy rate per treatment cycle, verified by the HFEA, and the national live birth rate and clinical pregnancy rate per treatment cycle)
- (f) the nature and potential risks of the treatment, including the risk of children conceived having developmental and birth defects
- (g) the possible side effects and risks to the woman being treated and any resulting child, including ovarian hyperstimulation syndrome (OHSS)

...

Information about the cost of treatment

4.3 Before treatment, storage or both are offered, the centre should also give the person seeking treatment or storage, and their partner (if applicable) a personalised costed treatment plan. The plan should detail the main elements of the treatment proposed (including investigations and tests), the cost of that treatment and any possible changes to the plan, including their cost implications. The centre should give patients the opportunity to discuss the plan before treatment begins.

...

Responsible use of the centre's website

4.5 In line with the Advertising Standards Authority's Code, the centre should ensure that the information provided on its website complies with the following guidance. This also applies to other relevant marketing communications of the centre and associated satellite and transport centres.

- a) The information should include the most recent data available from the past three years.
- b) The website should provide the live birth rate per treatment cycle, and not highlight a high success rate that applies only to a small, selected group of patients.
- c) The data should show split by maternal age and, if appropriate, by treatment type.
- d) The website should provide raw numbers rather than just percentages.
- e) The website should provide the national rate and like-for-like comparisons (the same year, maternal age, treatment type, etc.).
- f) The centre's published success-rate data should refer to the HFEA as the source of national information.
- g) The website must state clearly that information on success rates is of limited value in comparing centres and choosing where to seek treatment. It should include a link to the HFEA's advice on success rates: <http://www.hfea.gov.uk/fertility-clinics-success-rates.html>
- h) If the website refers to comparative costs, it should indicate the likely total cost for a typical cycle, based on the actual costs for recent patients, not individual items in tariffs.